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**Three-dimensional magnetic resonance imaging of the
pulmonary vascular system with rapid gradient echo acquisitions**

Wielopolski, Piotr Alfred, Ph.D.

Case Western Reserve University, 1992

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**THREE DIMENSIONAL MAGNETIC RESONANCE
IMAGING OF THE PULMONARY VASCULAR
SYSTEM WITH RAPID GRADIENT ECHO
ACQUISITIONS**

by

PIOTR A. WIELOPOLSKI

**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**

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THREE DIMENSIONAL MAGNETIC RESONANCE IMAGING OF THE PULMONARY VASCULAR SYSTEM WITH RAPID GRADIENT ECHO ACQUISITIONS

Abstract

by PIOTR A. WIELOPOLSKI

This dissertation demonstrates the utilization of 3-Dimensional Magnetic Resonance Imaging (MRI) incorporating magnetization prepared rapid gradient echo acquisition techniques in the study and assessment of the human pulmonary vascular system.

Among the several advantages that MRI offers, is its non-invasiveness which has attracted many researchers in the past decade to help characterize the cardio-pulmonary system. The impetus now taken by MRI in the diagnosis of the pulmonary system is directly related to its enormous flexibility to integrate and demonstrate excellent anatomic as well as physiologic information, possibilities not readily available with other clinical imaging modalities.

The utility of MRI in disease diagnosis in the thoracic region has been realized since its inception, yet the application of Magnetic Resonance Angiography (MRA) to visualize the pulmonary vasculature is a recent and yet unexplored approach for the assessment of pulmonary vascular disease.

The application of 3D techniques for the visualization of the pulmonary vascular tree is a major challenge for MRI. This is mostly due to the fact that the long data collection times involved in obtaining high resolution images leads to unavoidable image degradation, provided that thoracic motion is present. Despite this fact, the 3D approach allows for higher S/N, susceptibility artifact reduction with shorter echo times and isotropic data collection. The latter provides the benefit of multiplanar reconstructions (MPR) and a 3D visualization of the pulmonary vasculature using maximum intensity projections (MIP).

To study the pulmonary vascular system, two approaches have been considered. First, a proton density/inflow weighted scan based a syncopated 3D FLASH acquisition

is used to reconstruct a 3D angiogram of the pulmonary vascular tree. Secondly, a strong T_1 weighted 3D IR-FLASH acquisition reduces the signal from blood and enhances tissues with shorter T_1 values.

The latter technique has demonstrated great potential and high sensitivity for the diagnosis of pulmonary emboli in patients with suspected pulmonary embolism, a disease that is estimated to be the third most common cause of death in the United States. The 3D IR-FLASH technique makes it possible to visualize bright emboli against a suppressed vascular tree. Furthermore, the 3D IR-FLASH scan helped explain the pitfalls of the syncopated 3D FLASH technique to demonstrate vessel occlusion as signal voids, initially thought to compare with the views generated in standard contrast angiograms, the gold standard for the detection of pulmonary embolism. Using these techniques, it has been possible to discriminate clot from blood and follow a patient through treatment to visualize improvements in pulmonary vascular flow.

Multiple acquisitions and rectangular field-of-view are used to pseudogate to the respiratory period and reduce motion artifacts, while keeping reasonable imaging times. Technical aspects on data collection during the approach to equilibrium, acquisition strategies in the presence of thoracic motion and the impact on vessel resolution are addressed.

To my Parents

Acknowledgements

Probably the most enjoyable part of finishing this work of many years is thanking the people who made it possible. I would like to express my deepest appreciation:

To my thesis advisor Prof. E. Mark Haacke for his guidance and encouragement during the course of this work, the financial support provided for my studies and the everlasting enthusiasm for the education of all his students.

To Prof. Katherine Merritt for her constant interest in the project, as well as for the academic guidance during my graduate student years at Case Western Reserve University.

To Prof. Cecil Thomas for his clever comments, suggestions and hard hand in providing the right track for this work.

To Prof. Jean Tkach for her friendship, time, comments and devoted encouragement during the final stages of this dissertation.

To Dr. Lee Adler for all his time and efforts in providing the patients during the evaluation of this work as well for the continuous interest in the success of this project, and Dr. Alison Smith, for her time and suggestions.

I would also like to give thanks to the Biomedical Engineering department of Case Western Reserve University, and in particular:

To Prof. Gerald Saidel for helpful suggestions and the financial support received for many of the conferences attended throughout these years, and Donna Waldron for all her attentions.

I appreciate very much the support received from the Radiology department of University Hospitals of Cleveland and, in particular, I thank Joseph Moulter for the preparation of all the photographs appearing throughout this work as well for all the time spent these years providing all the photographic and presentation materials for papers and conferences. I also thank Charles Barrish for all the fun we had building some of the phantoms

used in many of the experiments performed. I value a lot the help provided from all the MR technologists during all this years and thank Mark Clampitt, Roberta Koss, Vicky Tabor, Louis Pittschmann and Betty Little, who made my stay very interesting at the MR facility.

I also thank all my other colleagues that helped me on many occasions with their knowledge and work. I would like to thank Sundar Amartur, James Goldfarb, Shantanu Kaushikkar, Ramesh Venkâtesan, Weili Lin, Daniel Finelli, M.D. and Debiao Li, Ph.D.

At last, I thank my friends Fatima and Fernando Boada for all their love and support, Cynthia Paschal for being a wonderful colleague and beloved friend, Robert Steagall for his computer expertise and Hubert Vesselle, for his interest in my well being during all these years.

Agradecimiento

No hay palabras que puedan describir mi agradecimiento y gratitud a aquellos que de alguna manera u otra apoyaron física y moralmente esta ardua empresa y permitieron que este trabajo floreciera.

En especial agradezco a mis padres, Jan y Wanda Wielopolski, por todo el esfuerzo y el inmenso cariño que demostraron durante todos los años de estudio.

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2D	two-Dimensional
3D	three-Dimensional
ADC	Analog-to- Digital Converter
B_1	RF excitation field with rotates the magnetization to the transverse plane. Usually applied along the x axis
B_{eff}	effective field
B_0	main magnetic field strength
CE-ROAST	Contrast Enhanced ROAST (see ROAST)
C/N	contrast-to-noise
Δt	sampling interval
$\Delta x, \Delta y, \Delta z$	spatial resolution in x, y and z
DFT	Discrete Fourier Transform
FFT	Fast Fourier Transform
FID	Free Induction Decay
FISP	Fast Imaging with Steady-state free Precession
FLASH	Fast Low Angle SHot
FOV	Field- of- View
FWHM	Full Width at Half Maximum
F_s	sampling frequency
G	gradient amplitude
GE	Gradient Echo
h	Planck's constant = $6.63 \cdot 10^{-34} \text{ J} \times \text{sec}$
$\hbar$	Planck's constant divided by 2π
Hb	Hemoglobin
IDFT	Inverse Discrete Fourier Transform
k	Boltzman constant = $1.38 \cdot 10^{-23} \text{ J/K}$
k-space	spatial frequency domain
k_x, k_y, k_z	spatial frequency domain variables
L_x, L_y, L_z	FOV in the x, y and z directions
M	bulk magnetization vector
M_0	thermal equilibrium value of the Magnetization
M_x, M_y, M_z	component of the Magnetization vector $\vec{M}$ in x, y and z
M_{xy}^+	transverse Magnetization after applying the RF excitation
M_{xy}^-	transverse Magnetization prior to the application of the RF excitation
MIP	Maximum Intensity Projection
MP	Magnetization Preparation period
MPR	Multi Planar Reconstruction
MP-RAGE	Magnetization Prepared RAPid Gradient Echo acquisition
MRA	Magnetic Resonance Angiography
N_x, N_y, N_z	points collected along the x, y and z directions
N_r, N_{pe}, N_{ss}	points collected along the frequency encoding, in-plane phase encoding and the slice select directions

MRI	Magnetic Resonance Imaging
NMR	Nuclear Magnetic Resonance
Partition	a slice generated from a 3D sequence
PEDD	Proton-electron Dipole Dipole Relaxation Enhancement
PSF	Point Spread Function
R	Relaxation rate
R_1	T_1 Relaxation rate
R_2	T_2 Relaxation rate
RBC	Read Blood Cell
RF	Radio Frequency
ROAST	Resonant Offset Averaged STeady state
R_x, R_y, R_z	spatial resolution in x,y and z
S/N	signal-to-noise ratio
T	Tesla. Magnetic field unit (1T = 10,000 gauss)
TI	Time of Inversion
TW	wait time
T_1	spin-lattice relaxation time
T_2	spin-spin relaxation time
T_2^*	effective transverse relaxation decay. $T_2^* = \frac{1}{1/T_2 + \gamma \Delta H_{ext}}$.
t_{ADC}	data acquisition window
TE	Echo Time
TH	slice thickness
TOF	time-of-flight
TR	Repetition Time
TR_{eff}	effective TR for each in-plane phase encoding step
T_s	sample temperature (K°)
t_y	duration of the in-plane phase encoding step
t_z	duration of the slice select phase encoding step
V_f	flow velocity
ω	angular frequency
ω_0	angular resonance frequency
α	RF excitation angle = $\gamma H_1 \tau_p$
α_{ERNST}	Ernst Angle. Angle for optimal signal in FLASH imaging
α_{opt}	Angle for optimal signal during the approach to equilibrium
β	resonant offset angle
γ	gyromagnetic ratio = $2.67 \cdot 10^8$ rad/sec/T
$\bar{\gamma}$	gyromagnetic ratio divided by 2π
$\rho(x, y, z)$	spatial proton density distribution
τ_p	RF application time

Chapter 1

Motivation and Background

Magnetic Resonance Imaging (MRI) is one of the most exciting imaging techniques and research tools in both clinical and biological research today. Since its inception, in the late 1970s, the technique has undergone a continuum of changes and has expanded its possibilities, directly emphasized by the close relation that this field guards with technological breakthroughs.

1.1 Motivation for Using Magnetic Resonance Imaging in the Diagnosis of the Pulmonary Vasculature

The advantage for which MRI is better appreciated for is its non-invasiveness. This has attracted many researchers in the past decade to characterize the cardio-pulmonary system and has helped demarcate the impetus that has now been taken by the technique in the diagnosis of the pulmonary system. This is the result of the enormous flexibility that MRI has in demonstrating and integrating excellent anatomic as well as physiologic information during a single sitting; possibilities not as readily available with other imaging modalities.

MRI is a good candidate for demonstrating the pulmonary vascular tree with the recent development of state-of-the-art MR angiographic techniques, which permit the non-invasive evaluation of the circulatory system.

The flexibility of MRI gives the potential for a multitude of evaluation and diagnostic

capabilities. General questions regarding pulmonary emboli [1, 2, 3, 4, 5, 6, 7, 8], pulmonary circulation, blood flow patterns and vessel distensibility [7, 9], lung parenchyma [10], clots [5, 6], deep venous thrombosis [11], hypertension [5, 7], flow quantification [7], congenital defects [12], chronic versus acute conditions [6] and dynamic imaging [5, 6, 13] have been evaluated with MRI. Patient follow up procedures after elective surgery or anticoagulant treatment can be easily performed non-invasively and may be accomplished as often as required [3, 4]. Although the administration of contrast agents has been explored to further enhance the pulmonary vasculature and parenchymal signal [10, 14], their potential use is still under evaluation. The multiple applications previously addressed indicate that MRI will play a major role in the evaluation of the pulmonary vasculature.

1.2 Pulmonary Vascular Physiology

1.2.1 Anatomical Considerations

The pulmonary vascular bed is very similar to the systemic circulatory system in that blood in the arteries, veins and capillaries are in a closed loop that starts and ends in the heart. The only difference compared to the systemic circulation is that pulmonary arteries carry deoxygenated blood whereas the pulmonary veins provide the oxygenated blood to the heart after having crossed the capillaries, where the gas exchange process in the alveoli is accomplished.

The main pulmonary wall and its two major branches have a thickness close to 30% of that of the aortic wall. The small arterioles, in contrast with the systemic circulation, are predominantly formed by endothelium with very little muscle content in their walls. The pulmonary capillaries are big and have multiple anastomosis, making each alveoli sit in a basket of capillaries.

1.2.2 Pulmonary Circulation: Pressure, Volume and Flow

The cardiac output from the right and left ventricle must be the same at any time, pumping approximately, under normal conditions, an average of 5.5 liters per minute at rest. Pulmonary ventilation is on the order of 4.2 liters per minute, thus giving a ratio of 0.8 between the pulmonary ventilation and the pulmonary blood flow.

The complete pulmonary system has the characteristics of a distensible system of low pressure. The pressure in the pulmonary artery is 24/9 mm Hg approximately with a mean pressure close to 15 mm Hg. The pressure at the input of the left atrium is close to 8 mm Hg during the diastolic phase, determining a pressure gradient of 7 mm Hg approximately across the entire pulmonary system, low compared to the pressure gradient of 90 mm Hg found in the systemic circulation.

The blood volume in the pulmonary vascular bed at any instance is close to a liter, from which less than 100 ml is contained in the capillary bed. The mean velocity of the pulmonary blood flow at the origin of the pulmonary artery is the same as the one in the aorta, approximately 40 cm/sec. Blood flow velocity decays rapidly, increasing slightly in the returning path through the pulmonary veins. A red blood cell takes generally around 0.75 sec to traverse the capillaries at rest, and 0.3 sec during exercise.

1.3 Vascular Diseases affecting the Pulmonary Vascular Tree

There are a host of diseases that may affect the pulmonary vascular system, congenital as well as acquired, that can have a profound effect on the hemodynamics of the pulmonary circulation. Congenital anomalies include those in which abnormal communications between the systemic and pulmonary circuits in the heart or great vessels are present: absence of the main pulmonary artery, anomalous venous drainage, patent ductus arteriosus, truncus arteriosus, large ventricular septal defect and transposition of the great vessels, among others. Acquired diseases include those in which blood flow through vessels is interrupted (pulmonary embolism) or pathological induced changes

affecting the vascular resistance during the onset of disorders that may or may not be directly associated with the pulmonary system (respiratory center failure, pneumonia, muscular dystrophy, poliomyelitis, or even residence at high altitudes).

The size of the pulmonary arterial trunk and its branches give an index of the pulmonary arterial pressure. In turn, the size of the more peripheral vessels is an indicator of the pulmonary blood volume and can be used to roughly indicate the pulmonary blood pressure and flow. Congenital as well as obstructive pathologic states usually produce an increase in the blood flow through the lungs, or increased resistance to blood flow to or its return from the lungs that is clearly imprinted in the appearance of the pulmonary vasculature during diagnosis using any imaging modality.

Section 1.3.3 and Section 1.4 will make a brief introduction to the effect of pulmonary emboli present in the arterial tree, and the current procedures used for the diagnosis of this disease. Its detection with magnetic resonance imaging techniques corresponds, in major proportion, to the thrust of this work.

1.3.1 The Normal Pulmonary Vessels

In a normal subject in an upright position, the smaller hydrostatic pressure at the lung apex makes the vessels going to this region have an extremely small caliber, in contrast to those vessels going to the lower lobes, usually of very much larger caliber. The vessels at midlevel have a slightly smaller caliber than those at the base.

When lying supine, all vessel calibers equalize and become comparable in all regions of the lung. In this position, the increase in the hydrostatic pressure in the upper lobes permits free perfusion to the upper lobe capillaries, which translates directly into an overall increase of the vessel caliber in this region.

1.3.2 Pulmonary Vessels and Cardiopulmonary Disorders

Among the vast variety of pulmonary diseases that may affect the pulmonary vasculature, pulmonary embolism, primary pulmonary hypertension, pulmonary artery

aneurysm, pulmonary arterial thrombosis, pulmonary arteriovenous malformations and pulmonary vasculitis/arteritis count among the pulmonary disorders that are directly related directly to those involving specifically the pulmonary arterial tree [15].

Figure 1.1: Diagrams of the right pulmonary vessels of an erect adult on frontal chest X-ray film. (a) Normal pulmonary vessels with larger vessels in the lower lung. (b) General caliber increase of pulmonary vessels typical of right-left shunts in congenital heart disease and high blood volume output states. (c) Distribution typical in chronic left heart failure with distended upper vessels and relatively smaller vessel towards the base of the lung. (d) Tortuous pulmonary arteries in severe pulmonary hypertension.

Figure 1.1 shows some of the changes that have been observed in the pulmonary arterial tree in plain X-ray film of the chest [16] with the onset of some of those

previously mentioned diseases that are not congenital in nature. These patterns are also likely to arise in congenital heart disease (CHD) and other heart diseases, congenital or acquired, that affect the heart itself as well as the pulmonary and systemic circuits.

1.3.3 Pulmonary Embolism

Among the numerous diseases that may affect the pulmonary vascular system, the occurrence of pulmonary embolism (PE) ranks among one of the most common and potentially life threatening disorders to the patient [2]. Pulmonary embolism is a pathologic process in which perfusion in some portions in the lung is compromised while normal ventilation to these regions is preserved (increased in the ventilation/perfusion (V/Q) ratio). The disease is clinically manifested by a sudden onset of arterial hypoxemia, hyperventilation, or pneumoconstriction in the embolized zones, secondary to the increased alveolar dead space and blood flow to the non-obstructed areas.

It is known that between 85% and 95% of the cases involving pulmonary embolism are the result of thrombus that originate deep in the lower-extremity venous system, promoted, in general, by stasis, injury to the intima of the venous wall and coagulation changes. Thrombus may also originate from the embolization of cerebral veins or from the left ventricle of the heart, which contained a thrombus once attached to its wall as a result from a myocardial infarction (wall thrombus). Other bodies such as fat emboli, tumor emboli, amniotic fluid and others can contribute to a smaller degree to the onset of pulmonary embolism. Macroemboli lodge in extra-alveolar pulmonary vessels whilst microemboli obstruct the pulmonary microcirculation.

Obstruction of the pulmonary arteries results in an increase in pulmonary vascular resistance, pulmonary pressure and right ventricular work. The larger the obstruction, the more acute the consequences, with the possibility for healthy individuals to suddenly and unexpectedly succumb or suffer from extensive cardiopulmonary deficit.

1.4 Diagnosis of Pulmonary Embolism

Pulmonary embolism is still considered a challenging diagnostic problem in the clinical realm. The clinical symptoms presented during the onset of pulmonary embolism mimic many other cardiopulmonary disorders [1] and no truly specific historical or physical findings are available upon which a diagnosis can be based firmly [8]. The respiration pattern induced depends on the severity of the obstruction, spanning from mild, transient dyspnea to severe breathlessness and syncope. In most cases, the former is the only symptom that regularly occurs and usually has a sudden appearance.

Chest X-ray examinations are obtained routinely on all patients suspected of pulmonary embolism. The chest X-ray is considered an essential part of the diagnostic imaging evaluation and remains to be the first imaging procedure performed to infer the possibility of the disease. This imaging modality is helpful in that it makes it possible to rule out other entities that may mimic embolism. Common signs seen include the presence of atelectasis, pleural effusions, infiltrates or an elevated hemidiaphragm, among others.

Nevertheless, further diagnostic evaluation is needed to determine the onset of pulmonary emboli. The other imaging modalities which provide a reasonable degree of sensitivity and reliability in the diagnosis are the scintigraphic ventilation-perfusion (V/Q) scan and pulmonary angiography.

The study most frequently performed is the V/Q scan. This is a noninvasive test in which pulmonary embolism can be diagnosed when two or more segmental perfusion defects (wedge shaped) in a segmental or lobar distribution and normal ventilation and no roentgenographic abnormalities on chest X-ray are identified. Normal V/Q scans rule out clinically significant pulmonary emboli. Positive scans can suggest a low and high probability for the disease but these are not reliable if not combined with the previous examinations mentioned. Often, the resulting V/Q scans are inconclusive [17, 18]. Any process that destroys or constricts the pulmonary arteries can also diminish the perfusion to particular regions and cause perfusion defects. This is the case of acute

obstructive airways disease or COPD, which may produce a pattern of focal perfusion abnormalities. Edema and alveolar secretions caused by lung infection will also produce perfusion defects.

In those cases in which the V/Q scans are in doubt in providing the final word in the diagnosis of the presence of pulmonary emboli, patients must undergo pulmonary angiography, still considered today the definitive diagnostic test for accurate disease detection [1, 2]. The latter procedure is highly invasive and is not without risk to the patient [19, 20], especially in those suffering from severe hypertension [20].

Pulmonary arterial branches appearing with filling defects or complete obstruction (abrupt vessel cutoff) are considered the two primary criteria for angiographic diagnosis of pulmonary embolism. Other frequent findings include partial obstruction of pulmonary arterial branches with increased caliber proximal and decreased caliber distal to the stenotic region and delayed or absent venous filling with contrast medium in those lung segments with obstructed arteries.

1.5 Statement of Problem

Three-dimensional (3D) magnetic resonance imaging techniques are considered a major challenge when high resolution images are to be acquired in regions where motion is present. In addition, long data acquisition times are characteristic in 3D imaging. Motion is particularly problematic in the thoracic region where the incessant work of the heart and respiratory muscles to keep us alive introduce unavoidable image degradation in the reconstructed images. Despite this fact, the 3D approach allows for higher S/N, susceptibility artifact reduction with shorter echo times and isotropic data collection. Isotropic data sets provide the benefit of multiplanar reconstructions (MPR) and processing of maximum intensity projections (MIP) that permits the reformation of the data in any desired orientation and complete three-dimensional views of the pulmonary vascular system.

The utility of MRI in disease diagnosis in the thoracic region has been realized since

its incorporation as a clinical diagnostic tool. The well established magnetic resonance angiography (MRA) techniques in routine use in the brain, neck, and peripheral vasculature studies have not been successful in generating consistently MR angiograms of the pulmonary system. Their application to this region of the body can be considered as a very recent and yet unexplored approach. There is still major hesitation for these techniques due to the inherent sensitivity of MRI to tissue motion which, in turn, leads to extensive image degradation. The recent thrust for MRA techniques in the evaluation of the pulmonary vasculature responds to the need for a reliable imaging approach, similar to X-ray contrast angiography in concept, but taking advantage of the non-invasiveness that only MRI can bring.

Nowadays, the major ongoing research in MR pulmonary angiography is directed to the optimization of MR angiographic sequences to demonstrate the presence of pulmonary emboli. This is not the only advantage to MR angiography and can be extremely useful in the study of the pulmonary vascular system in patients with congenital malformations and acquired diseases.

1.6 Overview of Dissertation Research

1.6.1 Specific Aims of the Research

The specific aims of this dissertation are the following:

1. Demonstrate the utility of fast 3D MRI techniques in the visualization and assessment of the pulmonary vasculature despite the physiologic motion occurring during data collection.
2. Evaluate different contrast possibilities with fast 3D gradient echo sequences using very short repeat times and echo times with and without magnetization preparation on the pulmonary vasculature of healthy and diseased individuals.
3. Determine the degree of enhancement possible with different k -space trajectories and data collection during the approach to equilibrium for “bright blood”

MR angiography using a syncopated excitation, validating the simulation results with stationary and flowing conditions in a flow phantom and on the pulmonary vasculature of healthy volunteers.

4. Investigate the filtering effects of the different k -space data collection schemes for the enhancement or suppression of blood and evaluate, subsequently, the effects on a vessel resolution and a flow phantom and on the pulmonary vasculature of healthy individuals.
5. Demonstrate qualitatively the effects of physiologic motion in the resolution of blood vessels under realistic imaging conditions.
6. Determine the potential utility of 3D angiographic sequences in the evaluation of obstructive diseases in the pulmonary vascular tree, such as pulmonary embolism, and discuss the possibilities for screening other pathologic states and irregularities.

1.6.2 Structure of the Dissertation

The dissertation has been organized in 12 chapters and a set of 4 appendices. This chapter has provided the motivation for pursuing MRI for the diagnostic of the pulmonary system, a brief review on the pulmonary anatomy and physiology, and an introduction to some of the pulmonary disorders that may affect the pulmonary vascular system and the potential appearance of the vasculature under these conditions. The aims of this dissertation and the relevant points to be addressed in subsequent chapters are also elucidated. Chapter 2 to Chapter 5 introduce the basics concepts of MR, MRI and MRA, concentrating in Chapter 4 on the acquisition strategies during the approach to equilibrium in fast imaging; these are more broadly developed in Chapters 6 and 7. These chapters cover different data collection strategies that help optimize the S/N and/or C/N, and the effects on the enhancement possible for flowing blood, respectively. Chapter 9 discusses the properties of blood and blood clots necessary to understand their signal behavior with different imaging protocols, followed by a comprehensive review of

the 2D pulmonary vascular approaches in the study of pulmonary embolism in Chapter 8. The application of the 3D techniques introduced in Chapter 4 culminates in Chapter 10 and Chapter 11 with the development and assessment of the experimental protocol used for the study of the pulmonary vasculature in healthy and diseased individuals. Finally, the conclusions of this work and future directions are addressed in Chapter 12. A set of appendices provide some background information for Chapters 2 to 5.

Chapter 2

Basics of Magnetic Resonance Imaging

Nuclear Magnetic Resonance, abbreviated NMR, was observed and characterized independently by the groups led by the two Nobel Prize recipients Bloch and Purcell in 1946 [21, 22]. Since then, NMR has been used extensively as an analytical tool in Physics and Chemistry for spectral analysis and the characterization of chemical compounds. NMR techniques have also been exploited to monitor metabolic reactions and have been widely used to elucidate the complex structure of organic molecules. Its final debut, in the late 70's, with its introduction in the medical field as Magnetic Resonance Imaging (MRI) has provided to the biological and clinical research one of the most versatile and powerful tools for the study of the anatomy and physiology of living tissue. It is characterized by its non-invasiveness, lack of ionizing radiation, high resolution capabilities and excellent soft tissue differentiation.

2.1 The Atom and Nuclear Magnetism

The basic structure of any living tissue is the atom and each atom contains three elementary particles: protons, neutrons and electrons. Hydrogen is an exception, it only contains a single proton and electron. Each elementary particle has its own intrinsic angular momentum or spin but only those atomic nuclei which present an odd number of protons or neutrons, nearly 2/3 of the stable nuclei, will exhibit a non-zero net spin. Since the nuclei contains electric charges and a spinning charge produces a

small circulating current, a small magnetic field is created. Consequently a magnetic moment $\vec{\mu}$ arises which is proportional to the angular momentum. The magnetic fields created by these magnetic dipoles are analogous to those of a microscopic bar magnet rapidly rotating about its own axes.

Since hydrogen with its single proton has a net magnetic moment, it confers to it the properties of magnetic resonance. Given its natural abundance in the form of water and nearly representing 70% of our total body weight, it is the nucleus that is most frequently exploited in medical MRI.

2.2 The Equilibrium Distribution: The Macroscopic Magnetization

When the magnetic dipoles are subjected to a static and uniform external magnetic field $B_o\hat{k}$, they will orient themselves with the line of induction of $B_o\hat{k}$ and the angular momentum, according to quantum mechanics, will become quantized. For the hydrogen proton, which has a spin $I=\frac{1}{2}$, there exists only two possible energy states, described as the Zeeman splitting of the energy levels, that makes the spins orient parallel or antiparallel to the external applied field.

At thermal equilibrium, the spin distribution can be calculated based on the Boltzman law. The ratio between the nuclei in the low energy level, $n_{parallel}$, to the high energy level, $n_{antiparallel}$, is given by

$$\frac{n_{parallel}}{n_{antiparallel}} = e^{\frac{\hbar B_o}{kT_s}} \approx 1 + \frac{\gamma \hbar B_o}{kT_s} \quad (2.1)$$

where k is the Boltzman constant, T_s the absolute temperature of the sample, $\hbar$ Planck's constant divided by 2π and γ the gyromagnetic ratio, expressing the ratio between the magnetic moment to the angular momentum (for protons $\gamma=2.67 \cdot 10^8 \frac{rad}{secT}$). Equation 2.1 indicates that there is a difference between both populations of spins with a slight excess of protons in the lower energy level. This excess is the one that gives rise to the macroscopic magnetization $\vec{M}$ of the sample when subjected to the external field

$B_0 \hat{k}$. The component of $\vec{M}$ along the field $B_0 \hat{k}$, M_z , is time independent and represents the projection of all the magnetic moments $\vec{\mu}$ of all the spins onto the axis of the field. Even though the transverse components are time dependent, they are randomly oriented since no field exists in this plane and the resultant magnetization is zero in this plane. Thus, the associated macroscopic moment per unit volume for hydrogen at equilibrium conditions is described by,

$$\vec{M}_0 = \frac{N\gamma^2\hbar^2 B_0}{V4kT_s} \hat{k} \quad (2.2)$$

where N indicates the proton population available in volume V . At the temperatures at which NMR experiments are carried on, the difference between states is very small. For example, at 1.5 Tesla (T), the fractional excess population in the lower level is approximately $1 \cdot 10^{-5}$ at room temperature, making it a very insensitive experiment. Nevertheless, because of the large abundance of hydrogen nuclei in biological systems (in water $\sim 10^{23}/cm^3$), proton NMR has been successfully adopted for MRI.

2.3 The Behavior of the Macroscopic Magnetization Vector

Nuclei placed in an external magnetic field $\vec{B}$ experience a torque on the magnetic moment $\vec{\mu}$ given by $\vec{\mu} \times \vec{B}$ and consequently the spins will aline with respect to $\vec{B}$. The equation of motion that drives the spins under this circumstance can be found by equating the torque applied with the rate of change of angular momentum, $\vec{J}$,

$$\frac{\partial \vec{J}}{\partial t} = \vec{\mu} \times \vec{B} \quad (2.3)$$

Since $\vec{\mu} = \gamma \vec{J}$, combining $\vec{J}$ into Equation 2.3 leads to

$$\frac{\partial \vec{\mu}}{\partial t} = \gamma \vec{\mu} \times \vec{B} \quad (2.4)$$

If the spins within the ensemble are assumed to be completely isolated from the environment and that no interaction exists between each other, we can replace $\vec{\mu}$ in Equation 2.4 by the measurable macroscopic moment $\vec{M} = \sum \vec{\mu}_i$, with a magnitude at thermal equilibrium conditions, M_0 , such as given earlier by Equation 2.2. Including the total contribution of all the magnetic moments of the spins in the ensemble allows Equation 2.4 to be written as

$$\frac{\partial \vec{M}}{\partial t} = \gamma \vec{M} \times \vec{B} \quad (2.5)$$

2.3.1 Resonance Frequency and The Resonance Phenomenon

The resultant torque that the external magnetic field $B_0 \hat{k}$ exerts on the magnetic moment $\vec{\mu}$ of each spin, makes the spin vectors precess around the axis of the magnetic field at an angular frequency ω_0 given by

$$\omega_0 = \gamma B_0 \quad (2.6)$$

resulting from the solution of Equation 2.5 when $\vec{B} = (0, 0, B_0)$. This precessional frequency is the frequency at which resonance occurs and it is known as the Larmor frequency. The relationship given by Equation 2.6 is linear and has been exploited extensively by MRI.

If enough energy in the form of radiofrequency (RF) waves is provided at the Larmor frequency, and this energy amounts to the difference in energy levels, ΔE , between the parallel and antiparallel population states

$$\Delta E = \gamma \hbar B_0 = \hbar \omega_0 \quad (2.7)$$

it will drive the population difference between the energy levels effectively to zero.

During the application of the RF excitation, Equation 2.5 can be written as

$$\frac{\partial \vec{M}}{\partial t} = \gamma \vec{M} \times [\vec{B} + \vec{B}_1(t)] \quad (2.8)$$

where $\vec{B}_1(t)$ represents the RF field. For the case in which $\vec{B}_1(t) = B_1(t)[\cos \omega_{rf}t\hat{i} + \sin \omega_{rf}t\hat{j}]$ and $\omega_{rf}=\omega_0$, the B_1 field is applied along the x -axis, $B_1\hat{i}$, when viewed in a rotating frame of reference rotating about the z -axis with an angular velocity $\vec{\Omega} = -\omega\vec{k}$. Depending on the amplitude of the B_1 field, the macroscopic magnetization vector $\vec{M}$ will be driven towards the y -axis in the transverse plane by an angle α defined by

$$\alpha = \gamma B_1 \tau_p \quad (2.9)$$

where τ_p is the application time of the RF field.

After the interaction disappears, the population difference returns back to its equilibrium condition given that, in practice, there are interactions between the spins and the surrounding media (lattice) and between spins that causes the energy absorbed to be dissipated in the lattice in order to regain the energy difference between levels at equilibrium conditions, and the magnetization in the transverse plane, M_{xy} , to disappear, respectively. The rate at which energy is dissipated in the lattice is characterized by the T_1 or spin-lattice relaxation time while T_2 , or spin-spin relaxation time, governs the disappearance of the transverse magnetization.

2.3.2 Observing the NMR Signal: The Free Induction Decay

The rotating magnetization vector in the transverse plane, M_{xy} , produces at the receiver end of an NMR spectrometer a signal proportional to the current induced in the receiver coil due to the change in magnetic flux through the latter (see Figure 2.1). Assuming that an angle α tilts partially the magnetization onto the transverse plane, the free induction signal known as the FID, is as expressed in the laboratory frame of reference is given by

$$M_y(t) = M_0 e^{-t/T_2} \cos(\omega_0 t) \sin \alpha \quad (2.10)$$

having assumed the B_1 field applied along the x -axis. The receiver electronics will demodulate this signal to baseband frequencies using a mixer frequency at ω_0 so that

the signal can be viewed as if a rotating frame of reference was being used (equivalent to dropping the $\cos(\omega_0 t)$ term from Equation 2.10).

In practice, the decaying FID does not follow the T_2 relaxation curve due to the presence of magnetic field inhomogeneities. These inhomogeneities, arising from magnetic field imperfections, magnetic susceptibility changes, chemical shift and the presence of ferromagnetic materials, among others, produces a faster decaying FID with an effective relaxation time T_2^* , such as defined by Equation 2.13 (see also Section 2.4.3). Thus, the exponential term of Equation 2.10 is usually replaced by e^{-t/T_2^*} , accordingly, to include this effect.

Figure 2.1: Free induction decay. The signal decays according to T_2^* due to the presence of field inhomogeneities

2.3.3 The Phenomenological Equations of Bloch

It is obvious that Equation 2.5 does not show any tendency for the magnetization to align again with the main magnetic field nor does it tend to disappear from the transverse plane. To account for the recovery of the magnetization along the z -axis and its disappearance from the transverse plane, Bloch included into Equation 2.5 the effects of the relaxation parameters T_1 and T_2 . T_1 describes the rate at which the longitudinal magnetization grows back to its thermal equilibrium value along the axis of the main

magnetic field. On the other hand, the decay of the transverse magnetization is related to T_2 , arising from the magnetic interactions between neighboring spins. Modelling the relaxation processes as a first order system, Equation 2.5 becomes

$$\frac{\partial \vec{M}}{\partial t} = \gamma \vec{M} \times \vec{B}_{eff} - (M_x \hat{i} + M_y \hat{j})/T_2 - (M_z - M_0) \hat{k}/T_1 \quad (2.11)$$

where M_x , M_y and M_z represent the components of the macroscopic magnetization vector $\vec{M}$, $\vec{B}_{eff}$ carries the effects of the RF excitation with $\vec{B}_{eff} = (B_0 - \frac{\omega_r}{\gamma}) \hat{k} + B_1 \hat{i}$, and M_0 represents the magnetization at thermal equilibrium conditions.

2.4 Relaxation Parameters

The intensity of the NMR signal recorded is not only related to the net magnetization of the sample but it is also strongly coupled with the molecular environment and the interactions occurring between the molecules within the sample. The relaxation parameters T_1 and T_2 included in the Bloch equations are the ones that provide the strongest contribution to the signal but many other sample properties can modulate the signal and be used to our advantage to better characterize the spin system.

2.4.1 The Longitudinal Relaxation Time: T_1

T_1 indicates the time constant for which the energy absorbed by the spin system during the RF irradiation is returned back or dissipated to the surroundings, or lattice, in the form of thermal energy. This loss of energy is known as the spin-lattice relaxation and describes the rate of return of the magnetization from its value after the RF excitation to its thermal equilibrium state, $M_0 \hat{k}$. This process is characterized by

$$M_z(t) = M_0(1 - e^{-t/T_1}) \quad (2.12)$$

and it can be thought of as the time necessary for the magnetization to regrow to 63% of its original value at thermal equilibrium or M_0 . T_1 also represents the characteristic

time for an unmagnetized ensemble of spins to build up the magnetization M_0 when first placed in a magnetic field.

The lattice fields arise from the presence of dipolar fields produced by other neighboring magnetic nuclei. In liquids, lattice field fluctuations are generally caused by random translational or rotational thermal motion of the molecules.

The size of the molecules plays an important role in determining the average rate at which molecules reorient. Smaller molecules tend to align more rapidly. Nevertheless, it is the frequency of rotation of the molecules in relation to the Larmor frequency that mainly determines the T_1 relaxation rate. The T_1 relaxation will be more effective when the lattice fields fluctuate at a rate that matches the Larmor frequency. T_1 increases with external magnetic field and indicates that the rotational frequency becomes slower relative to the increasing resonance frequency. The T_1 relaxation rate also depends on the number of protons which contribute to build up M_0 and the strength of the lattice fields at the resonance frequency.

T_1 relaxation is effective in medium sized molecules, such as lipids, since the frequency of rotation for these molecules closely matches the proton Larmor frequency at typical MR field strengths. Similarly, the relaxation process in macromolecules (proteins or DNA) is ineffective since their rotational frequency is much lower than the Larmor frequency. On the other hand, small molecules such as water have rotational frequencies much greater than the precessional frequency of protons and, consequently, they tend to have long T_1 relaxation times. The T_1 relaxation of solids becomes very long since given that a very small number of molecules rotate at the resonant frequency.

In biological tissues, water relaxes faster since the water molecule is bound to the surface of proteins. The rotational frequency of these protons is slowed by the presence of the macromolecule and as a result have shorter T_1 relaxation times than pure water. The values of T_1 range in tissues from about 50 msec to a few seconds, depending on their heterogeneity and the chemical and biological environment.

2.4.2 The Transverse Relaxation Time: T_2

After a system is excited, the transverse magnetization starts decaying with a time constant given by T_2 . This time constant is the consequence of spin-spin interactions and thus it has been denoted as the spin-spin relaxation time. The spin-spin interactions cause random fluctuations in the local magnetic field and hence produces a random change in the precessional frequency of each spin around the mean of the whole ensemble of spins, rotating at the Larmor frequency ω_0 .

This relaxation process does not involve any transfer of energy to the environment, making the process virtually independent of the strength of the external magnetic field.

Since T_2 is related to the intrinsic field caused by adjacent protons, the T_2 relaxation is more effective in large molecules since the rotation frequency is slower than that for smaller molecules and the magnetic interaction can be maintained for a longer period of time. In liquids, the T_2 relaxation times are long and can be on the order of seconds. Water molecules that are strongly bound to biologic macromolecules move more slowly and therefore they exhibit a reduction in T_2 . Thus, it is found in the body T_2 spanning from about 40 msec to several seconds, such as in cerebrospinal fluid.

In solids, T_2 is very short (in the order of μ secs) due to the fixed structure in solids, for which the local field variations are preserved for longer times and translate into a more rapid loss of transverse coherence.

2.4.3 T_2^* Relaxation

Spin-spin interactions are not the only sources that affect T_2 . In general, the decay of the transverse magnetization does not follow the predictions associated with solely interactions between spins. Magnetic field imperfections, magnetic susceptibility changes, chemical shift, the presence of ferromagnetic material, among others, affect T_2 such that the apparent relaxation time becomes shorter. These sources add phase incoherence within the ensemble at a much faster rate than those associated with T_2 . In general,

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \gamma \Delta B_{ext} \quad (2.13)$$

where T_2^* indicates the observed relaxation, always shorter than T_2 , and ΔB_{ext} combines all the effects from the sources listed above. Since the inhomogeneities are static, the loss associated with them can be recuperated by specific manipulations of the RF excitation on the spin system.

2.4.4 T_1 and T_2 Relaxation Times in Solutions with Paramagnetic Species

The presence of paramagnetic ions can provide a very effective mechanism for the enhancement of the T_1 and T_2 relaxation times. Paramagnetic ions have unpaired electrons and therefore have larger magnetic moments, approximately 700 times greater than that for protons (directly proportional to the ratio between the masses of a proton and an electron). The fluctuating fields are hence larger and will enhance the relaxation of protons for water molecules diffusing closely enough to the unpaired electrons. When the electronic magnetic moments fluctuate close to the Larmor frequency, the interactions are more effective and both T_1 and T_2 are shortened. This process is known as the proton-electron dipolar-dipolar (PEDD) proton relaxation enhancement (PRE). PEDD interactions are also referred to as “outer-sphere” relaxation effects. The strength of the interaction between the dipole of the electron and that of the hydrogen nucleus falls off as the sixth power of the distance that separates them and, therefore, hydrogen nuclei must be close to the paramagnetic center to have a strong effect on the relaxation times (within 3 Å). Scalar coupling or “inner-sphere” effects can enhance the paramagnetic relaxation when fluctuating fields are spanned during chemical exchange between the solvent and water ligands in which chemical bonds form or break.

The relaxation effects of paramagnetic substances are additive to the diamagnetic relaxation present and affect T_1 and T_2 to the same degree. Thus

$$R_{net} = R_{substance} + R_{paramagnetic\ agent} \quad (2.14)$$

where $R_{substance} = R_1$ or R_2 denote the reciprocals of the relaxation times T_1 and T_2 . Usually T_1 shortening dominates over T_2 shortening at the paramagnetic concentrations normally encountered.

2.5 Magnetic Susceptibility

The magnetic susceptibility χ , is a measure of how magnetized a substance can become under the influence of an external magnetic field. Thus

$$B' = (1 + \chi)B_o \quad (2.15)$$

where B' is the effective magnetic field observed. Most of the tissues are diamagnetic, χ is negative since all the electron spins are paired. On the other hand, paramagnetic substances have unpaired electron spins and present a positive χ .

2.6 Proton Density and Relaxation Parameters in Biological Tissues

Table 2.1 provides the proton density, T_1 and T_2 relaxation parameters of some of the tissues of interest that will be used for the simulations performed in subsequent chapters. The properties here displayed are those found for 1.5 T [23]. T_1 is somewhat shorter for all tissues at 1.0 T but T_2 remains fairly constant.

In regards to the tissue parameters of lung parenchyma, the water distribution and relaxation times are difficult to quantify due to the cyclic alterations of blood flow through the vessels, cardiac output, vascular permeability and the changes in position and inflation during respiration. The composition of lung is gravity dependent and this contributes to the complexity of the data interpretation. The various perfusion zones help create a continuous change in the lung composition from the least dependent to the

most dependent areas. Thus, the proton density and relaxation parameters are related to the proportion of blood in relation to air, lung tissue and interstitial fluid and differences should be expected depending on the measurement site. There is a large difference in the amount of blood present proportional to lung tissue and interstitial fluid in the least dependent areas when compared with that seen in the lower zones of the lung where the vasculature is distended with blood. This is demonstrated in Figure 2.2 (adapted from reference [15]). Table 2.2 demonstrates the gradients that have been statistically observed in normal lung parenchyma (from reference [15]).

tissue	fat	muscle	blood	white matter	grey matter	CSF
ρ	0.90	0.65	0.80	0.65	0.80	1.00
T_1 (ms)	284	800	1200	585	955	4500
T_2 (ms)	50	50	250	85	95	2200

Table 2.1: Spin Density, T_1 and T_2 relaxation times of some tissues of interest at 1.5 Tesla. CSF indicates Cerebrospinal Fluid.

A multiexponential transverse magnetization decay with a fast and a slow T_2 component has been demonstrated for normal peripheral lung tissue in rats [24]. The fast T_2 components were 9.5 ± 1.0 ms and 9.0 ± 1.5 ms for the right and left lung, respectively. The slow T_2 component in the right and left lung were 34 ± 5 ms and 32 ± 4.5 ms, respectively.

Figure 2.2: Blood distribution the lung in the supine position in relation to air, lung tissue and interstitial fluid content. Little perfusion is present in the least dependent areas. The capillary bed is dilated posteriorly and increases the ratio of blood to interstitial fluid and lung tissue.

	Zone I (anterior)	Zone II (laterally)	Zone III & IV (posterior)
signal intensity	100%	118.33% (21.92) p=0.007	205.41% (54.41) p=0.8579·10 ⁻⁶
ρ	100%	121.90% (23.02) p=0.067	186.88% (62.41) p=0.0005
T_1	100%	74.44% (23.14) p=0.006	71.68% (26.90) p=0.003
T_2	100%	140.71% (103.58) p=0.429	89.64% (67.17) p=0.697

Table 2.2: Statistically significant gradients of signal intensity, proton density, T_1 and T_2 seen in normal lung.

Chapter 3

Magnetic Resonance Imaging: MRI

An ensemble of spins in a sample under an ideal homogeneous magnetic field resonate at the same Larmor frequency. This indicates that when the NMR signal is formed after exciting the system with an RF field at the Larmor frequency, the signal will only contain information at the resonance frequency and hence the signal from one location of the sample cannot be distinguished from another nearby.

The Larmor equation indicates that the resonance frequency is linearly dependent on the applied magnetic field. This fact was first taken advantage of by Lauterbur [25], superimposing a linear magnetic field gradient on the main magnetic field. This caused a frequency spread around the resonance frequency, producing a spectrum proportional to the spin density distribution along the direction of the applied gradient field. This concept expanded, in principle, to all three orthogonal directions, can make the signal of a particular volume of spins in the sample unique by looking at its resonance frequency and phase. The latter statement constitutes the basis of magnetic resonance imaging.

3.1 Echo Formation

Practically, the NMR signal is viewed as an echo by either using spin echo (SE) or gradient recalled echo (GRE or GE) techniques. Here, only the mechanism of echo formation for GE sequences is addressed. First, the concepts of spin isochromat, resonance frequency in the presence of a gradient field and the phase accumulated due

to the presence of an inhomogeneous magnetic field are briefly reviewed.

3.1.1 Spin Isochromats

All spins start precessing from the same location on the transverse plane after the RF excitation is applied. In practice, spins do not experience the same magnetic field strength making some of them precess faster than others if the effective magnetic field seen by those spins is higher, hence a higher resonance frequency, or slower, if the opposite case applies, while the ensemble rotates at a mean resonance frequency given by ω_o . A spin isochromat is defined by that group of spins that experience the same magnetic field strength and will have the same resonance frequency and evolution in time given that a set of external conditions are applied.

3.1.2 The Resonance Frequency Under the Presence of a Linear Gradient Field

Simultaneous application of the gradients in all three orthogonal directions produces an effective magnetic gradient field during time t , $\vec{B}_{eff}(t, x, y, z)$, superimposed on the main magnetic field $B_o \hat{k}$ given by

$$\vec{B}_{eff}(t, x, y, z) = B_o \hat{k} + G_x(t)x\hat{i} + G_y(t)y\hat{j} + G_z(t)z\hat{k} \quad (3.1)$$

viewed in the laboratory frame of reference and where $G_x(t) = \frac{\partial B_z(t)}{\partial x}$, $G_y(t) = \frac{\partial B_z(t)}{\partial y}$ and $G_z(t) = \frac{\partial B_z(t)}{\partial z}$ represent the time varying gradient fields applied in x, y and z , respectively.

Grouping the gradient contribution into a single gradient vector $\vec{G}(t) = G_x(t)\hat{i} + G_y(t)\hat{j} + G_z(t)\hat{k}$, the effective magnetic field given by Equation 3.1 can be rewritten as

$$\vec{B}_{eff}(t, \vec{r}) = [B_o + \vec{G}(t) \cdot \vec{r}] \quad (3.2)$$

with location (x, y, z) represented by the vector $\vec{r} = x\hat{i} + y\hat{j} + z\hat{k}$. Consequently, the resonance frequency at location $\vec{r}$ is given by

$$\omega(t, \vec{r}) = \gamma[B_o + \vec{G}(t) \cdot \vec{r}] \quad (3.3)$$

Equation 3.3 indicates that two samples contained in a plane perpendicular to the applied gradient field will experience the same resonance frequency and cannot be distinguished.

3.1.3 Phase Accumulation

The fact that some spins precess at different rates with respect to ω_o , makes each spin isochromat deviate more and more from its neighboring spins as the time goes on. Each isochromat can be viewed as a vector changing its direction on the transverse plane according to the field it experiences. The angle that the vector forms with respect to its original position, in the rotating frame of reference, can be interpreted conveniently as the phase accumulated by that isochromat as it evolves in time.

The phase difference between two spin isochromats, denoted as $\Delta\Phi_f$, is proportional to the difference between the resonance frequencies experienced and hence magnetic fields. Denoting the difference in magnetic fields as ΔB_{ext} (see Section 2.4.3), the phase induced as a function of time at position $\vec{r}_o = x_o\hat{i} + y_o\hat{j} + z_o\hat{k}$ is given by

$$\Delta\Phi_f = \gamma \int_0^t \Delta B_{ext}(\vec{r}_o) dt \quad (3.4)$$

In the case of an FID experiment, the vectorial addition of different isochromats leads to the observation of the NMR signal decaying according to T_2^* .

When the linear gradients applied for imaging are included as part of ΔB_{ext} , their sole contribution to the phase of the isochromats can be represented in general terms as

$$\Phi_G = \gamma \sum_{i=1}^{i=n} \int_{t_{i1}}^{t_{i2}} \vec{G}_i(t) \cdot \vec{r}_o dt \quad (3.5)$$

where Φ_G results from the addition of all the gradient events, denoted by $\vec{G}_i(t)$, applied in x , y and z during the times t_{i1} and t_{i2} that each gradient event is active.

3.1.4 Echo Formation using Gradient Recalled Echoes

In the presence of an applied gradient field, an echo is formed when the phase contribution of the negative gradient is cancelled by the phase contribution of the positive gradient event, such as shown in Figure 3.1.

Figure 3.1: Signal formation for a GE sequence. The phase accumulation created by the dephasing gradient is cancelled by the rephasing gradient to form an echo at TE (a). When field inhomogeneities are present, a constant gradient term given by ΔB_{ext} is added that changes the position at which the echo may occur, indicated by TE' in (b). FE indicates the field echo time, the relative time of echo occurrence for a specific gradient structure.

The echoes formed by gradient reversal lack the inherent refocusing properties that RF pulses have for the SE sequences (RF echo) and cannot compensate for the presence of field inhomogeneities. The phase induced by the latter continues to accumulate for longer echo times. The phase at t_4 is given in this case by

$$\Phi_a(t_4) = \gamma[\Delta B_{ext}t_4 - G(t_2 - t_1) + G(t_4 - t_3)] \quad (3.6)$$

with the timing according to the diagram of Figure 3.1. This implies that spins experiencing different ΔB_{ext} will refocus at different times (indicated by TE' in Figure 3.1b, with the echo forming at the end of the sampling window). This can lead to a major phase dispersion across a voxel (volume element), that may cause complete signal cancellation or signal enhancement as well.

3.2 Spatial Encoding

As mentioned earlier, the NMR signal has no inherent spatial information. The application of the linear magnetic field gradients with a vector component along a direction of interest, makes it possible to identify each spin location on the basis of different resonance frequencies. Ideally, the gradient field should produce a linear change in frequency across the imaging region but, in practice, this linearity is only possible over a limited range.

After having applied an RF field, the portion of the magnetization rotating in the transverse plane will generate an FID or an echo according to the sequence of RF and gradient pulses used as discussed in Section 3.1.4. For an FID that has been demodulated to baseband by $e^{i\omega_0 t}$, the signal received, $S(t)$, can be expressed as

$$S(t) = \iiint \rho(x, y, z) e^{-t/T_2^*(x, y, z)} dx dy dz \quad (3.7)$$

which represents the response of the spin density distribution $\rho(x, y, z)$ at the resonance frequency ω_0 decaying with the spatially dependent filter associated with $T_2^*(x, y, z)$.

The signal $S(t)$ as it stands in Equation 3.7, does not have any spatial information associated to it. The use of a gradient field will directly associate a location with a particular resonance frequency, and the strength of the signal at that frequency is directly related to the proton density at that location. Assuming a spin density distribution varying along one particular direction, i.e., a variation along the x coordinate, $S(t)$ becomes under the presence of a gradient field applied in x , G_x ,

$$S(t) = \int \rho(x) e^{-i\gamma G_x x t} e^{-t/T_2^*(x)} \Delta V_y(x) \Delta V_z(x) dx \quad (3.8)$$

where $\Delta V_y(x)$ and $\Delta V_z(x)$ represent the contribution to the signal from the projection of all the spins available along the y and z coordinates. Note that the frequency content of $S(t)$ will depend on the value of x

$$\text{frequency content of } S(t) = \bar{\gamma} G_x x \quad (3.9)$$

which will be proportional to the gradient applied and the size of the object imaged with $\bar{\gamma}$ indicates the gyromagnetic ratio divided by 2π . It is common to refer to the domain of the signal $S(t)$ as k -space, after $S(t)$ is transformed from an analog signal to a digital one. When G_x is a square gradient pulse, it is convenient to make the substitution $k_x = \bar{\gamma} G_x t$ such that Equation 3.8 becomes

$$\tilde{S}(k_x) = \int \rho(x) e^{-i2\pi k_x x} e^{-t/T_2^*(x)} \Delta V_y(x) \Delta V_z(x) dx \quad (3.10)$$

where $\tilde{S}(k_x)$ represents the quantized version of $S(t)$. This expression corresponds to what is known as the imaging equation for a one-dimensional experiment. Recognizing that Equation 3.10 has the form of a Fourier Transform, an Inverse Discrete Fourier Transform (IDFT) applied over $\tilde{S}(k_x)$ can provide the discrete estimate of the spin density, namely $\hat{\rho}(x_i)$, such that

$$\hat{\rho}(x_i) = V_y(x \pm \frac{\Delta x}{2}) V_z(x \pm \frac{\Delta x}{2}) \rho(x \pm \frac{\Delta x}{2}) * \mathcal{F}^{-1}[e^{-t/T_2^*(x)}] \quad (3.11)$$

represents the true spin density $\rho(x)$ convolved with the IDFT of $e^{-t/T_2^*}(x)$, a Lorentzian line. $\hat{\rho}(x_i)$ concentrates the spin density contained in $x_i \pm \frac{\Delta x}{2}$ with Δx depending on the imaging reconstruction parameters and the strength of the gradients during the encoding of $S(t)$.

3.2.1 The Concept of K-space

K-space has been denoted as the spatial frequency domain and it represents the signal domain before an Inverse Discrete Fourier Transform is applied to view the spin density distribution. The spatial frequencies are a measure of the number of sine wave cycles per unit length of an object and hence, high values of k -space characterize the smaller details in the image.

The integral description of the k -space variables is given by

$$k_x = \gamma \int G_x(t) dt \quad (3.12)$$

$$k_y = \gamma \int G_y(t) dt \quad (3.13)$$

$$k_z = \gamma \int G_z(t) dt \quad (3.14)$$

For example, to resolve an object in three dimensions, points along k_x , k_y and k_z must be collected, as explained in subsequent sections. Recently, many schemes have been devised to collect k -space to either reduce image acquisition times, allow for more flexibility in S/N and image contrast manipulation or a combination of both. Further discussion has been reserved to Chapter 6, in which the benefits and drawbacks of different k -space collection patterns are discussed in the context of pulmonary imaging.

3.2.2 The Multi-dimensional Imaging Equation

The concept illustrated by Equation 3.10 can be expanded to encode the spin density $\rho(x, y, z)$ for all three axis. By using the integral definitions of the k -space variables as defined in Equation 3.12, the complete imaging equation in MRI is given by

$$\tilde{S}(\vec{k}) = \iiint \rho(\vec{r}) e^{-i2\pi\vec{k}\cdot\vec{r}} W(\vec{r}, T_1, T_2) H(\vec{r}, \vec{k}) d\vec{r} \quad (3.15)$$

where $\vec{k} = (k_x, k_y, k_z)$, $W(\vec{r}, T_1, T_2)$ corresponds to the weighting that the appropriate imaging experiment will have on the proton density at each location in the object, and $H(\vec{r}, \vec{k})$ includes the effects of external factors on the final intensity of the image such as the presence of field inhomogeneities (T_2^*), signal variation during the acquisition and motion, among others.

To reconstruct a 2D or 3D data set, the gradient field varies as a function of time to encode all the values of k -space required. Gradients are switched for a certain amount of time to define the phase for each point (x, y, z) in the imaging volume.

3.3 The Imaging Process

3.3.1 Volume Selection

A volume selection is performed in order to encode the spin density of a certain region of interest. The selection process can be done spatially selectively or non selectively, depending on the presence or absence of a slice selection gradient, namely G_{ss} . In the selective case, the RF is chosen with a frequency bandwidth that translates directly to the thickness of the excited slice in the presence of a predefined value of G_{ss} . To produce signal after the selective excitation, a refocusing gradient must be applied after the RF is terminated to equalize the phase of all the spins. For a non selective excitation, no external gradient is applied. Hence, the entire volume imaging volume is excited and the slice defined will have the thickness of the object. The RF pulse is generally referred to as a hard pulse.

3.3.2 The Frequency Encoding

For a one-dimensional object spanning along the x direction from $-\frac{L_x}{2}$ to $\frac{L_x}{2}$

$$\rho(x) = \begin{cases} 1 & \text{for } -\frac{L_x}{2} \leq x \leq \frac{L_x}{2}, \\ 0 & \text{elsewhere} \end{cases} \quad (3.16)$$

the object is said to be contained in a field-of-view (FOV) of L_x and the signal $S(t)$ will have a maximum frequency content given by

$$\text{maximum frequency content of } S(t) = \bar{\gamma} G_x \frac{L_x}{2} \quad (3.17)$$

Since the signal $S(t)$ is sampled discretely every Δt sec during this encoding process, the Nyquist relationship indicates that the sampling frequency, F_s , must be at least equal or greater than twice the frequency content of $S(t)$ to avoid aliasing. Thus,

$$F_s = \bar{\gamma} G_x L_x \quad (3.18)$$

which in terms of the k -space variable k_x ,

$$\Delta k_x = \bar{\gamma} G_x = \frac{1}{L_x} \quad (3.19)$$

with $\Delta t = \frac{1}{F_s}$. Since only a limited number of samples are collected, the acquisition window t_{ADC} will be given by

$$t_{ADC} = N_x \Delta t \quad (3.20)$$

where N_x indicates the number of points collected along x direction to reconstruct the object with a desired resolution. The process here described corresponds to what is known as the frequency encoding. It permits the visualization of the projection of the proton density distribution along the gradient field during the signal readout defined after having performed an IDFT on the sampled version of $S(t)$.

3.3.3 Phase Encoding: The Two-Dimensional and Three-Dimensional Experiments and K-space Sampling Relationships

The simultaneous application of all gradients produces a linear frequency variation only along the vector that the gradient field defines. Points in a plane perpendicular to that vector resonate at the same frequency and thus cannot be distinguished.

In order to reconstruct a two-dimensional or three-dimensional description of the proton density distribution, $S(t)$ must be phase encoded along the two orthogonal directions to the frequency encoding gradient, denoted here as G_r .

In order to perform a 2D experiment, two gradients orthogonal to each other are applied to encode the “in-plane” information after the volume selection process is completed. One axis of k -space is sampled along the frequency encoding direction during the acquisition of $S(t)$. The other dimension is encoded by incrementing the phase contribution of a gradient, namely G_{pe} , for each acquisition of $S(t)$. This is done since it is not possible to resolve a 2D image with a single value of G_{pe} . This process is known as the in-plane phase encoding, and the number of steps, N_{pe} , needed to resolve the sample will depend on the in-plane resolution desired. In general, the amplitude of G_{pe} is incremented by ΔG_{pe} , keeping the time of gradient application, t_{pe} , at a constant value.

If G_x is selected for the frequency encoding process, the y gradient, G_y , is usually assigned as the in-plane phase encoding gradient while G_z for the slice select encoding. The phase encoding time is defined as t_y and the number of phase encoding steps required N_y , accordingly.

Assuming N_x points sampled along the frequency encoding, setting $N_x=N_y$ and an in-plane FOV given by L_x and L_y , the in-plane phase encoding gradient increment, ΔG_y , is defined according to the Nyquist criteria as

$$\Delta G_y = \frac{1}{\gamma t_y L_y} \quad (3.21)$$

$$\Delta t = \frac{1}{\bar{\gamma} G_x L_x} \quad (3.22)$$

which in terms of k -space

$$\Delta k_x = \bar{\gamma} G_x \Delta t = \frac{1}{L_x} \quad (3.23)$$

$$\Delta k_y = \bar{\gamma} \Delta G_y t_y = \frac{1}{L_y} \quad (3.24)$$

The resolution in the x and y directions, R_x and R_y , respectively, are then given by

$$R_x = \frac{L_x}{N_x} \quad (3.25)$$

$$R_y = \frac{L_y}{N_y} \quad (3.26)$$

The image formation for a 3D experiment is, in essence, an extension of the 2D imaging concept. Figure 3.2 depicts a basic 3D sequence diagram. To resolve the third direction, a phase encoding process is performed along the slice select direction to generate N_z slices, or partitions, after having excited a volume usually thicker than that of a 2D experiment.

Having the frequency encoding gradient along the x -axis and the in-plane phase encoding along the y -axis, the slice select phase encoding is applied along the z -axis. To resolve the slice select direction, the phase encoding process is repeated N_z times using a varying G_z during its application time, t_z , to generate N_z slices. To comply with the Nyquist criteria, the FOV used in this case is defined by the thickness of the volume selected, L_z . This defines ΔG_z as

$$\Delta G_z = \frac{1}{\bar{\gamma} L_z t_z} \quad (3.27)$$

with

$$\Delta k_z = \bar{\gamma} \Delta G_z t_z = \frac{1}{L_z} \quad (3.28)$$

Consequently, if N_z partitions are acquired, the resolution along the slice select direction, R_z , will be given by

$$R_z = \frac{L_z}{N_z} \quad (3.29)$$

Figure 3.2: 3D experiment. After volume selection, the 3D partitions are encoded using a phase encoding table along the slice select direction. The in-plane information is encoded by sampling the signal $S(t)$ during the application of the frequency encoding gradient G_r and repeated N_{pe} times to encode the 2D image by stepping the phase encoding gradient G_{pe} . To encode N_{ss} slices, the process is repeated for each value of G_{ss} .

3.3.4 Rectangular Field-Of-View (RecFOV)

RecFOV is a useful feature that makes it possible to increase the resolution along the in-plane phase encoding direction when the object is confined to a smaller region than the predefined FOV along this direction for the number of phase encoding lines selected. Another possibility permits to decrease the imaging time by maintaining the resolution while decreasing the number of phase encoding lines. Taking L_y as the FOV selected

and S_y the maximum extent of the object along the in-plane phase encoding direction, then

$$R_y = \frac{S_y}{N_y} \quad (3.30)$$

which indicates that the resolution can be increased by the ratio $\frac{L_y}{S_y}$ before starting to incur into aliasing problems and breaking the Nyquist relationship. The maximum phase encoding increment allowed, $\Delta G_y \text{ max}$, is then given by

$$\Delta G_y \text{ max} = \frac{1}{\gamma t_y S_y} \quad (3.31)$$

This indicated that the new phase encoding increment is defined by $\frac{L_y}{S_y} \Delta G_y$, where ΔG_y is the originally defined phase encoding step (Equation 3.21).

To reduce the imaging time but keeping the same resolution, the number of phase encoding lines collected can be reduced by a factor of $\frac{S_y}{L_y}$. The image is then interpolated down by the same ratio $\frac{L_y}{S_y}$ after the Fourier transform is applied.

3.3.5 Imaging Times

The imaging time required to obtain a 2D image given that a single in-plane phase encoding step is acquired per TR, is determined by

$$\text{Imaging time 2D} = N_y \cdot N_{acq} TR \quad (3.32)$$

where N_y indicates the number of in-plane phase encoding steps and N_{acq} , the number of acquisitions. Similarly, the extra phase encoding required for 3D imaging along the slice select increases the imaging time by the number of slices or 3D partitions, N_z , selected

$$\text{Imaging time 3D} = N_z N_y N_{acq} TR \quad (3.33)$$

In special cases where more than one phase encoding value is acquired during TR, the imaging time is reduced, accordingly, by the number of phase encoding steps acquired, N_s . Thus,

$$\text{Imaging time}' = \frac{\text{Imaging time}}{N_s} \quad (3.34)$$

3.4 Fast Imaging Sequences

3.4.1 The Steady-State

The steady-state regime is generally referred to those NMR experiments in which the magnetization is subjected to a pulsed RF irradiation with an interpulse interval shorter than the T_1 and T_2 of the sample imaged.

During steady-state, two distinctions can be made depending on the treatment imposed over the longitudinal and transverse magnetization during the execution of a particular imaging sequence structure. The general derivation of the steady-state equations (see Appendix B) was done by considering that the pulsing interval was set to be much shorter than T_1 and T_2 , and a constant resonant offset β , remained between RF pulses.

Sequences can be classified as steady-state coherent (SSC) and steady-state incoherent (SSI), respectively depending on the treatment of the transverse magnetization (i.e. gradients and RF phase) before each excitation. This distinction is introduced since the approach to equilibrium and signal characteristics for both is quite different (T_1 vs T_1/T_2 weighted) and is essentially determined by the absence or existence of transverse magnetization before the next RF pulse.

Only the FLASH sequence structure will be addressed here since it constitutes the structure that was used for all the experiments performed in this work.

3.4.2 FLASH Imaging

FLASH (Fast Low Angle SHot) [26, 27] is an SSI GE sequence that was first introduced in the clinical scenario with the main objective of providing T_1 weighted images in a fraction of the time that took SE sequences to generate the same contrast. This was accomplished by choosing a shorter TR while optimizing the signal with the use of partial flip angles. An example 3D FLASH structure is shown in Figure 3.3.

Figure 3.3: Diagram of a basic FLASH sequence for 3D imaging. Spoiler structures based on randomized gradient tables or application of RF spoiling to eliminate transverse coherences for short TR provide a signal proportional to the longitudinal magnetization recovered between adjacent RF excitations.

The primordial condition for this sequence is to have the transverse magnetization completely eliminated (via irreversible dephasing) before the application of the next RF excitation. Under this condition, the signal behavior is given by setting the variable E_2 in the solution of the Bloch equations for a steady-state regime be equal to zero (see Equation B.9 in Appendix B). The signal for the transverse and longitudinal

magnetization components prior to and after the RF excitation are given by

$$M_x^- = M_x^+ = 0 \quad (3.35)$$

$$M_y^- = 0 \quad (3.36)$$

$$M_z^- = \frac{M_o(1 - E1)}{(1 - E1 \cos \alpha)} \quad (3.37)$$

$$M_y^+ = \frac{M_o(1 - E1) \sin \alpha}{(1 - E1 \cos \alpha)} \quad (3.38)$$

where $E1 = e^{-TR/T_1}$. The transverse magnetization M_y^+ has only contributions from the longitudinal magnetization recovered during the interpulse interval between RF excitations. Thus M_y^+ is formed strictly by the steady-state longitudinal magnetization.

3.4.3 Optimal Flip Angle and Signal for FLASH Imaging

The optimal flip angle for FLASH imaging is known as the Ernst angle [28] and it is given by the relationship

$$\alpha_{ERNST} = \cos^{-1}(e^{-TR/T_1}) = \cos^{-1}(E1) \quad (3.39)$$

For fixed TR (with $TR \ll T_1$, the optimum flip angle decreases as T_1 increases. The signal at the Ernst angle becomes

$$M_y^+ = \frac{(1 - E1)^{\frac{1}{2}}}{(1 + E1)^{\frac{1}{2}}} \quad (3.40)$$

Chapter 4

The Approach To Equilibrium in Fast Imaging with Magnetization Prepared Gradient Echo Acquisitions

Back in 1946, Bloch [21] proposed his famous phenomenological equations of motion to model the dynamics of the macroscopic magnetization vector in a sample immersed in a static magnetic field and subjected to a constant, time varying electromagnetic field near the resonance frequency. It was almost a decade later, when Carr in 1958 [29] demonstrated in his early experiments the effects of a periodic pulse excitation with an oscillating RF field coherent from pulse to pulse. He noted that the spin system approached a steady-state condition where the behavior of the magnetization vector was constant from pulse to pulse. More recently, it has been observed that images acquired during this transient behavior can, in principle, define signals for tissues and hence, the contrast available is dramatically different from acquisitions during steady state conditions.

This Chapter discloses the behavior of the magnetization for a spin system starting from thermal equilibrium conditions or a predefined initial magnetization as it evolves towards steady-state. The concept of syncopated and magnetization prepared acquisitions is extended to 3D imaging since they make it possible to encode a specific tissue contrast that may better depict the presence of a disease, based on the more sensitive management of the initial longitudinal magnetization prior to data collection.

4.1 The Approach to Equilibrium

The magnetization of a spin system experiences a dynamic evolution when driven by a string of RF pulses, stabilizing, in the limit, to an equilibrium condition. The characteristics of the magnetization signal during the approach to equilibrium is dependent on the type of imaging sequence and imaging parameters (mainly flip angle and TR) chosen to sample the signal, and the tissue parameters T_1 and T_2 .

For repetition times shorter than the T_2 of the tissues imaged, the approach to equilibrium is rather complex and the signal formed is a mixture of transverse and longitudinal magnetization components which regain coherence at every RF excitation. Depending on the sequence structure chosen, the signal during the approach to equilibrium will only contain the longitudinal magnetization or will reflect the contribution of both the longitudinal and transverse magnetization components.

The approach to equilibrium for steady state incoherent (SSI) sequences (FLASH) will be formed exclusively from the longitudinal magnetization component recovered between RF excitations. On the other hand, steady state coherent (SSC) sequences (FISP, ROAST and CE-ROAST), make use of the longitudinal and transverse magnetization to form the signal [23].

Transverse magnetization components in SSC sequences can be taken advantage of during the approach to equilibrium to boost the S/N. Nevertheless, spin motion modifies the SSC signal to have an SSI behavior similar to FLASH. Consequently, SSC sequences will not be able to maintain the transverse coherence for blood spins: their motion produces different resonant offsets and dephasing prior to every RF excitation. The SSC regime can only persist when stable phase conditions for each spin are maintained over a considerable number of RF excitations. The approach to equilibrium for SSC sequences will not be treated here but a discussion on its behavior has been reserved to Appendix C.

4.1.1 The Approach to Equilibrium for SSI: FLASH

The signal calculation during the approach to equilibrium for a FLASH sequence is straightforward, assuming that only longitudinal magnetization recovered between RF pulses contributes to the signal formation and all the transverse magnetization has been previously eliminated prior to the application of the next RF excitation. The assumption is reasonably valid for moving tissues [30, 31] and it can also hold true if RF spoiling techniques are used [32, 33] (see Section 4.1.3).

The longitudinal magnetization after the application of the n th RF pulse, $M_z^+(n)$, is given by

$$M_z^+(n) = M_z^-(n) \cos \alpha \quad (4.1)$$

Prior to the next RF pulse, the longitudinal magnetization, $M_z^-(n+1)$, can be written as

$$M_z^-(n+1) = M_z^+(n)E1 + M_o(1 - E1) \quad (4.2)$$

where M_o denotes the thermal equilibrium magnetization, α the RF flip angle and $E1 = e^{-TR/T_1}$. A recursive formula for $M_z^-(n)$ for the n th can be derived by substituting Equation 4.1 into Equation 4.2

$$M_z^-(n) = M_o[(E1 \cos \alpha)^{n-1} + (1 - E1)\sum_{i=0}^{n-2} (E1 \cos \alpha)^i] \quad (4.3)$$

for $n \geq 2$. The transverse magnetization, M_y^+ , immediately after the n th RF pulse is given by

$$M_y^+(n) = M_z^-(n) \sin \alpha \quad (4.4)$$

Recognizing that the summation in Equation 4.3 is the representation of a finite geometric series of the form

$$\sum_{i=0}^n ar^i = \frac{a(1 - r^{n+1})}{1 - r} \quad (4.5)$$

yields,

$$M_y^+(n) = M_0 \sin \alpha [M_s(1 - r^{n-1}) + r^{n-1}] \quad (4.6)$$

with $r = E1 \cos \alpha$, $M_s = (1 - E1)/(1 - r)$ and valid for $n \geq 1$. Evaluating the limit for $n \rightarrow \infty$, Equation 4.6 converges to the well known signal at equilibrium conditions for FLASH imaging

$$M_y^+ = M_0 \sin \alpha \left[\frac{1 - E1}{1 - E1 \cos \alpha} \right] \quad (4.7)$$

FLASH is characterized by having a smooth approach to equilibrium, with a monotonic decrease in signal with increasing RF excitation number. The speed at which equilibrium is approached depends strongly on the product $r = E1 \cos \alpha$. The rate of convergence will be slower for a combination of imaging and tissue parameters that make r closer to unity. The limiting case for which the approach to equilibrium is the slowest is the case of very short TR , very low flip angles (1° - 3°) and long T_1 . Taking blood with $T_1 = 1200$ ms, $TR = 8.2$ ms and $\alpha = 2^\circ$, equilibrium is reached in approximately 400 RF excitations within 5% of the final value (however, its starting value is only 9% away from the equilibrium value). For higher flip angles, i.e., greater than 70° , most tissues reach equilibrium after a few excitations (values of r closer to zero). In the latter case, the number of excitations needed to stabilize the system becomes independent of the repeat times used. Figure 4.1a,b demonstrate the approach to equilibrium for cerebrospinal fluid (CSF), blood, muscle and fat for a fixed TR and two different flip angles.

The influence of a longer TR is demonstrated in Figures 4.2 a,b, for the same flip angles utilized in Figures 4.1a,b, respectively. For tissues with T_1 much longer than TR , an increase in TR when low flip angles are used shortens the approach to equilibrium proportionally.

The effects of slice profile imperfections are not included in the calculations. This is not necessary for 3D imaging, since each slice encoded in the 3D volume may be considered to have a uniform excitation profile. The influence of the RF profile on the

approach to equilibrium has been treated extensively for 2D acquisitions [34].

Figure 4.1: Approach to equilibrium for cerebrospinal fluid (CSF), fat, muscle and blood for a FLASH sequence with $TR=8.2$ ms and a flip angle of 5° (a) and 20° (b), respectively.

Figure 4.2: Approach to equilibrium for cerebrospinal fluid (CSF), fat, muscle and blood for a FLASH sequence with $TR=20$ ms and a flip angle of 5° (a) and 20° (b), respectively.

4.1.2 The Effects of Motion

Transverse coherences are dependent on having a constant resonant offset, β , from pulse to pulse. Failing this condition, the approach to equilibrium will not build in a

coherent fashion and the signal will approach the SSI behavior. Thus, the echo signal will only be determined by the signal from the longitudinal magnetization recovered between RF pulses.

Figure 4.3: Approach to equilibrium for blood in SSC sequences with a linear increment of the resonant offset angle. (a) SSC ideal behavior, (b) $\Delta\beta=45.5^\circ$, (c) $\Delta\beta=117^\circ$ and (d) SSI behavior (FLASH). For blood, $T_1=1200$ ms, $T_2=250$ ms.

The resonant offset changes if thermal diffusion, flow or motion is present in the system, along with any change in the sequence structure from pulse to pulse (see Appendix C). Figure 4.3 shows the effect of a linear change in β from pulse to pulse to demonstrate the case in which the approach to equilibrium is mostly affected by spin motion. During a situation of constant flow, the increment in β can be directly related to the flow velocity and the particular set of gradients applied during imaging.

It is worth pointing out that when imaging with SSC sequences at the Ernst angle, M_y^+ is independent of β and, hence, the signal behaves exactly like FLASH for any

tissue under any condition. Nevertheless, the strength of M_x is related to the value of β which makes M_{xy}^+ have the same dependence.

4.1.3 Spoiling

There are many mechanisms by which the transverse magnetization prior to an RF excitation can be eliminated. Section 4.1.2 demonstrated the effects that a change in resonant offset produces to the SSC signal when spins move. If motion is not present, changes from cycle to cycle of the repetition time, phase contribution of gradients prior to the RF, RF phase [32] or RF frequency [33] will produce the same effect by imparting a controlled phase increment to each spin isochromat before the next RF pulse. This will preclude the coherent addition for the transverse magnetization from one pulse to the next [35, 36] and avoid its contribution at the RF time. While all the methods mentioned before contribute to spoil the transverse magnetization, the latter two are the only ones that are independent of the spin position and make it possible to change the phase of every isochromat by the same amount (recall that the phase accumulation of a spin under the effects of a gradient field are dependent on the position of the spin). Thus, the use of large and constant gradient pulses, or gradients with random or linearly incremented amplitudes will only spoil the transverse magnetization partially, leaving a central banding artifact in the image. Computer simulations demonstrated that an increment in phase of 117° was optimal for RF spoiling using a ROAST sequence (for which the phase of the isochromats is constant from cycle to cycle). RF spoiling is demonstrated in the simulations of Figure 4.3 using a 45.5° and 117° phase increment for each cycle. Natural spoiling is achieved if tissues with short T_2 are imaged with long TR since the natural decay of the magnetization before the next RF pulse suffice to avoid the buildup of transverse coherences.

4.2 Modification of the Natural Approach to Equilibrium with a Magnetization Preparation Stage

4.2.1 Contrast Encoding with Magnetization Preparation

In general, images collected with FLASH with low flip angles during the approach to equilibrium lack tissue contrast. They show a proton density mixed with a slight T_1 weighting that will depend on the flip angles used. For example, to increase the T_1 weighting, higher flip angles may be employed at the expense of higher RF deposition and increased artifacts in the images due to transverse coherences, increased motion artifacts and inadequate management of the signal from blood. Higher flip angles are also irrelevant in this case since their use will destroy the contrast that can be obtained during the approach to equilibrium.

To change the contrast and maintain low flip angle imaging, a magnetization preparation (MP) period has been proposed [37, 38] and applied prior to data collection to encode a desired contrast. A sequence element consisting of a gradient and RF pulsing scheme similar to those structures used for each in-plane phase encoding in standard SE sequences encodes the desired contrast before the application of the short TR gradient echo sequence that samples the prepared magnetization. This has proven useful to obtain similar contrast characteristics to 2D SE and inversion recovery (IR) techniques. These techniques have assumed the acronym MP-RAGE [38] for Magnetization Prepared Rapid Acquisition Gradient Echo sequence. Some of the MP structures that have been used are shown in Figure 4.4.

To increase the T_1 weighting, an inversion pulse is introduced to affect the initial longitudinal magnetization prior to data collection using a very short TR , 2D FLASH imaging sequence acquiring all N_{pe} in-plane phase encoding steps. This is demonstrated in Figure 4.4d, where the MP period is represented by the shaded block in the diagram.

The treatment to calculate the signal is analogous to the one described for the approach to equilibrium without the magnetization preparation structure. For an inversion

time TI , the longitudinal magnetization prior to the first RF pulse in the train is given by the well know expression,

$$M_z^-(TI) = M_0(1 - 2E_{TI}) \quad (4.8)$$

with $E_{TI} = e^{-TI/T_1}$. The expression for the transverse magnetization for the first string of RF pulses applied to the spin system is given by

$$M_y^+(n) = M_0 \sin \alpha [M_s(1 - r^{n-1}) + (1 - 2E_{TI})r^{n-1}] \quad (4.9)$$

valid for $n \geq 1$ and where $r = E1 \cos \alpha$ and $M_s = (1 - E1)/(1 - r)$.

Figure 4.4: Magnetization preparation (MP) structures for short TR gradient echo imaging. The MP stage can consist of a simple 180° preinversion pulse (IR like) for T_1 weighting (a), a 90°_x - 180°_y - 90°_x driven equilibrium pulse scheme for T_2 weighting (b) (with and without the addition of diffusion sensitizing gradients) or fat suppression pulses (c). For a 2D IR-FLASH acquisition, the 180° inversion pulse is applied and after an inversion time, TI , the signal is read by a short TR 2D FLASH sequence (d).

4.3 3D Magnetization Prepared Gradient Echo Acquisitions

4.3.1 Signal and Approach to Equilibrium for a 3D Syncopated FLASH Experiment

For a syncopated experiment, a wait period, TW , is included after a finite number of RF excitations, N , to introduce a longitudinal magnetization recovery before stepping to the next readout period. When the FLASH imaging structure is used, the signal can be calculated following closely the steps previously considered in the derivation of the approach to equilibrium for FLASH in Section 4.1.1.

The longitudinal magnetization prior to each string of N RF pulses is given by

$$M_z^-(k, 1) = M_z^-(k-1, N) \cos \alpha E_{TW} + M_o(1 - E_{TW}) \quad (4.10)$$

where $E_{TW} = e^{-TW/T_1}$. The convention taken here is that the first index in the parenthesis, k , indicates the number of the RF pulse train while the second index, N , indicates the RF pulse number within each train. The effect of the application of n th RF pulse in the k th RF pulse train is found to be

$$M_z^-(k, n) = M_z^-(k, 1)r^{n-1} + M_o M_s(1 - r^{n-1}) \quad (4.11)$$

with $r = E1 \cos \alpha$, $M_s = (1 - E1)/(1 - r)$ and valid for values of $k \geq 1$ and $n \geq 1$. The previous expression is used to derive the transverse magnetization for a k th RF string for any RF excitation n within the string.

$$M_y^+(k, n) = M_o \sin \alpha \{ M_s(1 - r^{n-1}) + [(1 - M_s)A + BC + M_s]r^{n-1} \} \quad (4.12)$$

with

$$A = (qr^{N-1})^{k-1}$$

$$B = 1 - E_{TW} - M_s(1 - q)$$

$$C = \frac{1 - (qr^{N-1})^{k-1}}{1 - qr^{N-1}}$$

valid for $k \geq 1$ and with $r = E_1 \cos \alpha$ and $q = E_{TW} \cos \alpha$. When the syncopated excitation is considered for a 3D sequence, as depicted in the diagram of Figure 4.5, the variable k is analogous to any of the in-plane phase encoding steps and n relates to one of the RF excitations utilized to encode the N slice select phase encoding steps or partitions.

Figure 4.5: Diagram for a syncopated FLASH acquisition. For each in-plane phase encoding line, k , the frequency encoding and all slice select phase encoding steps, N , are acquired using a very short repeat time, low flip angle FLASH sequence, followed by a recovery time TW . TW is used to adjust the saturation of stationary tissue.

The introduction of TW generates two approaches to equilibrium after data acquisition starts. One approach occurs during the collection of the frequency encoding and the slice select phase encoding steps for every in-plane phase encoding line. The other is the approach to equilibrium of the initial magnetization at the beginning of each in-plane phase encoding line (see Figure 4.6).

The latter stabilizes after the collection of several phase encoding lines and will be faster if longer TW 's are chosen between in-plane phase encoding lines, higher flip

angles are used or a large number of partitions is collected. This approach does not affect the contrast significantly.

Figure 4.6: The approach of the starting value of each RF string and the approach during the RF string. The simulation is done for blood using a $TR=8.2$ ms, $TW=200$ ms, $\alpha=7^\circ$ and $N=32$ for $k=1$ to $k=8$.

The plot in Figure 4.7 depicts the effects of TW on the approach to equilibrium for blood. In the simulation, blood is assumed to be stationary. In practice, the enhancement will depend on blood flow rates and pulsatility (as discussed in depth in Chapter 7). The blood is also compared in Figures 4.8a,b to the surrounding tissues found in the thoracic region for a finite TW and two different flip angles, respectively.

The system reaches a steady-state response after having applied several strings of RF pulses. The complex expression introduced in Equation 4.12 transforms into

$$M_y^+(k, n) = M_o \sin \alpha (M_s(1 - r^{n-1}) + Tr^{n-1}) \quad (4.13)$$

with

$$T = \frac{M_s q (1 - r^{N-1}) + 1 - E_{TW}}{1 - q r^{N-1}}$$

Figure 4.7: Approach to equilibrium for blood for different values of TW . Maximum signal for blood occurs when spins previously saturated are replaced by freshly magnetized blood spins during a finite TW . The latter condition corresponds to the case of $TW=\infty$, demonstrated by the thicker line in the graph. The simulation is done using a $TR=8.2$ ms, $\alpha=7^\circ$ and $N=128$.

In the limit of very long TW , Equation 4.13 converges to the expression for the approach to equilibrium from thermal equilibrium conditions as dictated by Equation 4.6.

Figure 4.8: Difference in signal between fresh blood as compared to fat, muscle and blood remaining in the excited slab for $TW=500$ ms, $TR=8.2$ ms, $N=128$ and $\alpha=7^\circ$ (a) and $\alpha=14^\circ$ (b), respectively. The dashed line indicates the signal for fresh blood entering the slab during TW . For blood: $\rho=0.8$, $T_1=1200$ ms; fat: $\rho=0.9$, $T_1=284$ ms; muscle: $\rho=0.65$, $T_1=800$ ms.

4.3.2 Including a Wait Time in IR-FLASH: 3D IR-FLASH

An extension of the syncopated FLASH concept can also be introduced for the 2D IR-FLASH sequence by incorporating TW between phase encoding cycles to create the 3D IR-FLASH sequence (originally introduced as MP-RAGE [38]). The magnetization dynamics are similar to those described in the previous section but includes the inversion pulse into the calculation. A diagram of a 3D IR-FLASH acquisition is shown in Figure 4.9

Figure 4.9: Diagram for a 3D IR-FLASH acquisition. For each in-plane phase encoding line, k , the frequency encoding and all slice select phase encoding steps, N , are acquired after having applied a 180° pulse that inverts all the spins before sampling the magnetization using a very short TR , 3D FLASH sequence, followed by a recovery time TW .

The inclusion of TW generates an approach to equilibrium such as previously described in Section 4.3.1 for each in-plane phase encoding (refer to Figure 4.6). This is demonstrated for a 3D IR-FLASH acquisition in Figure 4.10.

Note from Figure 4.10 that the zero crossing point for blood changes dynamically until it reaches a stable value. For a small number of excitations and short TW it takes several cycles to reach this stable period. The same remarks of Section 4.3.1

can be made here: longer TW , higher flip angles and a large number of partitions will contribute to make the approach to equilibrium in the in-plane phase encoding direction to be reached for the 2nd RF string.

Figure 4.10: The approach of the starting value of each RF string and the approach during the RF string for 3D IR-FLASH. The simulation is done for blood using a $TR=8.2\text{ms}$, $TW=200\text{ ms}$, $\alpha=7^\circ$ and $N=32$ for $k=1$ to $k=8$. TI was chosen accordingly at 125 ms to null the signal at the 16th RF pulse of each string at steady state conditions.

The signal during steady state conditions for any k^{th} RF string has been derived previously [39] and it is given by

$$M_y^+(k, n) = M_o \sin \alpha (M_s(1 - r^{n-1}) + Hr^{n-1}) \quad (4.14)$$

with

$$H = \frac{E_{TI}[-M_s q(1 - r^{N-1}) + E_{TW} - 2] + 1}{1 + E_{TI} q r^{N-1}}$$

Equation 4.14 is derived by setting the magnetization at a particular excitation during the RF string to be equivalent to the latter in all the different RF strings so that a steady state regime is forced.

Figure 4.11: Signal for IR-FLASH 3D with $TR=8.2$ ms, $\alpha=12^\circ$ $TW=200$ ms and $TI=290$ ms, chosen to null the blood signal after 7 RF pulses (C_8) were acquired.

Figure 4.11 compares the magnetization behavior among different tissues. For the parameters chosen, muscle and blood have a similar zero crossing which will produce an image where blood and muscle are similarly suppressed. Fat never has a zero crossing due to its short T_1 and will always appear bright in the reconstructed image.

Figure 4.12 demonstrates the variation of TI with TW to null out blood for a sequence encoding 128 partitions and 3 different points during the RF string. It is worth mentioning here that in experiments in which TW may change dynamically during the acquisition (i.e. cardiac triggered acquisitions), TI will also change accordingly. This indicates that the choice of TI during physiological imaging will depend on the heart rate of the subject and thus, a search for the optimum TI to null out the signal from a tissue will be set by trial and error.

Figure 4.12: Inversion times for blood in a 3D IR-FLASH experiment as a function of TW and the number of RF pulses applied before the collection of the central Fourier line, where blood signal is zeroed out. The sequence parameters used to determine TI were: $TR=8.2$ ms, $N=128$ and $\alpha=12^\circ$. No value for TI can be found for the range displayed for a sequential ordering of k-space, for which 63 RF pulses are applied

Only for sequential acquisitions using very low flip angles (1° - 5°), very short TR , and practically a TW on the order of $5T_1$, the TI needed to provide a zero crossing at

the central phase encoding line can be roughly calculated with the relation $TI + TR \frac{N}{2} = T_1 \ln 2$. Larger angles, longer TR and short TW will make the TI for signal suppression lower and TI can be calculated according to Equation 4.14. The labels C_0 , C_8 and C_{16} refer to the number of RF pulses applied prior to sampling the signal (refer to Section 6.2).

Figure 4.13: Inversion times for blood for a fixed $TW=300$ ms and varying flip angle with a $TR=8.2$ ms, $N=128$ and 7 and 15 RF preparation pulses. When a gaussian RF profile is utilized to readout the signal, each partition in the 3D volume will have effectively a different flip angle and consequently a different TI . The change is fairly linear for blood and scales down uniformly when a larger number of RF preparation cycles are used for the ranges utilized.

In practice the excitation profile is not uniform and the varying flip angles will produce a different zero crossing for blood for a fixed TW . The inversion time changes as a function of TW almost in a linear fashion in the range shown in this example. TI

must be reduced when TW is shortened and the number of RF pulses applied prior to the collection of the center of k-space is increased.

Figure 4.13 demonstrates the TI needed to zero out blood for different flip angles, $TW=300$ ms and $N=128$, assuming that 7 and 15 RF preparation pulses are applied before data collection.

As shown in Figure 4.13, the change in TI is fairly linear for blood and scales down when a larger number of RF preparation cycles are used. The example here demonstrates the variability and sensitivity of the null point for blood or other tissues of interest. In practical situations, significant variation can be found for the flip angle across the excited volume, given that the excitation profiles are usually not ideal and far from being rectangular.

4.4 Summary

This chapter has explored the behavior of a spin system during the approach to equilibrium for a FLASH sequence starting from thermal equilibrium, or a predefined longitudinal magnetization encoded with a magnetization preparation (MP) period prior to data collection. The approach to equilibrium was then analyzed for magnetization prepared acquisitions suited for 3D imaging and used to characterize the behavior for a synopated 3D FLASH experiment using only a wait time TW prior to encoding the slice select data, and a 3D IR-FLASH experiment, in which a 180° inversion pulse was applied accordingly to introduce strong T_1 weighting. The form of the equations driving the transverse magnetization during the approach to equilibrium is essentially the same for the 2D and 3D techniques discussed. The equations combine a term that depends on the number of RF pulses applied and the value of the longitudinal magnetization prior to the string of RF pulses, and a constant term that represents the FLASH signal at steady-state conditions.

Chapter 5

Concepts in Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) is a relatively new area in magnetic resonance imaging capable of demonstrating vascular information non-invasively. The technique is yet considered a screening procedure and it continues to be one of the areas of most active research today.

The visualization of the vascular tree has been possible thanks to the sensitivity of the MR signal during the presence of motion. This sensitivity has been known for decades in flowing liquids and dates back to the times of continuous wave excitation [40]. Depending on the design of the imaging experiment, amplitude or phase changes in the MR signal can be taken advantage of to characterize flowing blood.

In this chapter, some basic concepts in magnetic resonance angiography are introduced.

5.1 Bright Blood Magnetic Resonance Angiography Techniques

Blood motion can be used to our advantage in many different ways in order to demonstrate vascular structures. The family of angiographic sequences in use today can be grouped into two major categories: the “white blood” techniques, in which blood is enhanced against stationary tissue, and “black blood” techniques, in which blood is sup-

pressed. “White blood” techniques can be further subdivided into time-of-flight (TOF) and phase contrast angiography. Many techniques have been used to eliminate blood in the “black blood” techniques but its significance for pulmonary imaging is minimal since lung parenchyma has a very low signal and this would not lead to blood/tissue contrast.

5.1.1 Time-of-flight MRA

Time-of-flight MRA allows the visualization of the vascular tree by enhancing the differences in signal amplitude between blood and surrounding stationary material.

The time-of-flight effect is better demonstrated for blood entering perpendicular to the imaging volume. During the application of the imaging sequence, tissue remaining within the imaging volume experiences the effects of the RF excitation during the length of the imaging experiment and its signal will remain at a constant value given that an equilibrium condition has settled at a value lower than its original value at thermal equilibrium. The latter condition can be referred to as spin saturation. Blood not previously excited enters the imaging volume and replaces previously excited spins by fully magnetized spins. This allows for those spins to deliver the maximum signal possible for the excitation angle used. Blood saturation can also occur, particularly in a 3D experiment, as the spin travels through the excitation region. The rate at which saturation is approached downstream depends on the imaging parameters used.

5.2 Phase Shifts due to Motion

During the imaging experiment, the imaging gradients applied to spatially encode the MR signal introduce a different phase shift for each spin according to Equation 3.5. The phase accumulated by each spin is related to its location, its state of motion and, in particular, to the gradient waveform applied during the signal encoding. To account for motion effects in Equation 3.5, a temporal dependence is introduced to the spatial variables x , y and z as described in Section 5.2.1.

5.2.1 Spin Motion

The position of a spin as a function of time, $r(x, y, z, t)$, can be characterized by expanding the spin motion trajectory in three independent Taylor series

$$\begin{aligned} r(x, y, z, t) &= [x_o + v_x t + \frac{1}{2}a_x t^2 + \frac{1}{6}j_x t^3 + \dots \frac{1}{n!}m_{xn}t^n]\hat{i} \\ &= [y_o + v_y t + \frac{1}{2}a_y t^2 + \frac{1}{6}j_y t^3 + \dots \frac{1}{n!}m_{yn}t^n]\hat{j} \\ &= [z_o + v_z t + \frac{1}{2}a_z t^2 + \frac{1}{6}j_z t^3 + \dots \frac{1}{n!}m_{zn}t^n]\hat{k} \end{aligned} \quad (5.1)$$

where x_o , y_o and z_o represent the initial position of the spin at instant zero and $v_{x,y,z}$, $a_{x,y,z}$ and $j_{x,y,z}$ describe the velocity, acceleration and jerk components, respectively. Higher motion components can be included if the Taylor expansion is continued to describe the n^{th} motion moment, represented by m_{xn} , m_{yn} and m_{zn} for the different orientations, respectively. If periodic motion is present, the motion components will also have a time dependence. Nevertheless, if the data acquisition period is comparatively shorter than the motion itself, the motion components can be treated as being time independent.

5.2.2 Phase Accumulation During Motion

Motion is introduced into the imaging equation (Equation 3.15) as an additional complex exponential term that provides the phase accumulated by a spin as it moves through the changing gradient field.

Evaluating the k-space Fourier variables defined in their integral form (Equations 3.12) and using the motion description of Equation 5.1, the phase accumulation for each axis as a function of time is given by

$$\begin{aligned} \Phi_x(t) &= \gamma \int G_x(t) [x_o + v_x t + \frac{1}{2}a_x t^2 + \frac{1}{6}j_x t^3 + \dots] dt \\ \Phi_y(t) &= \gamma \int G_y(t) [y_o + v_y t + \frac{1}{2}a_y t^2 + \frac{1}{6}j_y t^3 + \dots] dt \\ \Phi_z(t) &= \gamma \int G_z(t) [z_o + v_z t + \frac{1}{2}a_z t^2 + \frac{1}{6}j_z t^3 + \dots] dt \end{aligned} \quad (5.2)$$

which fully describes the effects that the gradient waveforms applied in x , y and z during an imaging experiment will have on the resulting signal.

The extra phase accumulation due to motion is thus integrated into the 3D imaging equation to yield

$$S(t) = \iiint \rho(x, y, z) e^{-i2\pi(\Phi_x(t) + \Phi_y(t) + \Phi_z(t))} W(T_1, T_2, x, y, z) dx dy dz \quad (5.3)$$

where $W(T_1, T_2, x, y, z)$ provides the spatial weighting to the proton density according to the signal characteristics of the imaging experiment performed.

5.3 Motion Compensation Gradients

Motion can create a major phase dispersion across the imaging voxel at the time of the echo and destroy the possible signal received due to intravoxel phase cancellation. Ghosting artifacts can also arise when phase cancellation is not complete, and the resulting phase at a particular location changes from one phase encoding value to the next. Such phase changes commonly occur during imaging of regions in the body in which motion occurs. Phase dispersion can be maximally minimized by using the concept of motion compensation by gradient waveform design [41]. The number of gradients used to eliminate motion will depend on the number of moments that want to be nulled. Thus, the set of equations that must be satisfied at the time of the echo, TE , are given by

$$\begin{aligned} \Phi_x(TE)_i &= 0 \quad \text{for } 0 \leq i \leq n \\ \Phi_y(TE)_i &= \gamma \int G_y(t) y dt \quad \text{for } 1 \leq i \leq n \\ \Phi_z(TE)_i &= 0 \quad \text{for } 0 \leq i \leq n \end{aligned} \quad (5.4)$$

given that x , y and z represent the frequency encoding, phase encoding and slice select, respectively, and n representing the number of moments to be zeroed out. In general,

for the slice select and frequency encoding axes, $n + 1$ gradient lobes need to be applied to eliminate the phase contributions for motion containing up to the n^{th} moment. For the phase encoding only n gradient lobes are used since the 0^{th} moment needs to have a finite phase contribution to allocate the phase encoding process. Moments not compensated for will introduce a non-linear phase during sampling that is manifested as a complex filter convolved with the final image [41].

5.4 Phase Dispersion for Short TE

Short TE 's have been recently employed to accommodate imaging techniques using very short TR 's. Typically, the simple bipolar gradient structure demonstrated in Figure 3.1 and asymmetric data collection, with 16-45 points collected before the echo, are used to allow for TE 's ranging between 2-3.5 ms, capable of handling small FOV imaging. Since this gradient waveform is not compensated for velocity and other higher motion terms, phase dispersion at the echo for moving spins can lead to signal loss. Using an expression for the the pulsatile velocity waveform in the aorta [42] (similar to that at the pulmonary artery), the phase dispersion due to velocity and acceleration for the typical trapezoidal gradient waveforms utilized along the frequency encoding axis are demonstrated in Figures 5.1c,d as a function of time. Figures 5.1a,b show the velocity and acceleration waveforms in the aorta utilized for a cardiac period of 1 sec, respectively.

The phases are evaluated with the expressions for the phase contribution of trapezoidal gradients waveforms found in Appendix D. It has been assumed that the gradient waveform is applied after turning off the RF excitation (typically 320 μsec from the center of the RF in all the experiments performed) and the number of points is increased to achieve longer echo times with both the dephasing and rephasing gradient lobes having the same gradient amplitude. The maximum phase contribution along the slice select is approximately 0.14 radians for a 640 μsec RF applied during a 2 mT/m slice select gradient and a peak velocity of 90 cm/sec.

Figure 5.1: Velocity (a) and acceleration (b) waveforms in the aorta and phase dispersion due to velocity (c) and acceleration (d) along the frequency encoding axis for a simple bipolar, trapezoidal gradient waveform. 16, 32 and 48 points are collected before the echo and the gradient waveform is applied $320\mu\text{sec}$ after the center of the RF. These correspond to echo times of 2.21 ms, 2.85 ms and 3.49 ms, respectively. A 256 mm FOV and a $20\mu\text{sec}$ sampling rate were selected, defining a 4.588 mT/m gradient for both the dephasing gradient and the gradient during the signal readout. $500\mu\text{sec}$ ramp times were used.

Chapter 6

Signal Response and Resolution During the Approach to Equilibrium

Fast imaging was introduced to speed up acquisition time and at the same time maintain the comparable contrast characteristics as standard SE scans yet maintain S/N. Initially, decreasing the acquisition time was possible with the introduction of partial flip angle excitation in order to optimize the signal with shorter repeat times.

Nowadays, not only partial flip angle is used to manipulate the signal. Contrast and S/N optimization have taken a completely different approach with data collection during the transient state between thermal equilibrium conditions and steady-state. This transient response not only can be modified with a convenient choice of imaging parameters but also taken advantage of with different concepts of k -space traversal.

The order in which k -space lines are collected does not affect, in general, image contrast and resolution when 2D or 3D data sets are acquired after a steady-state response has been reached. Nevertheless, data collection during the approach to equilibrium introduces a different magnetization for each phase encoding step that can potentially translate into resolution loss or enhancement and/or signal-to-noise gains when different k -space trajectories are considered during the acquisition.

This chapter analyzes the signal strength during the approach to equilibrium and discusses several k -space ordering strategies and filtering effects associated during the optimization of the S/N and contrast. Simulations and experimental results on a vessel

resolution phantom are demonstrated.

6.1 Quantifying the Enhancement During the Approach to Equilibrium

The transition between thermal equilibrium and steady-state conditions can be taken advantage of to enhance the signal of ultra-short TR scans. When SSI scans such as FLASH are used for imaging during steady state conditions with ultra-short TR , considerable spin saturation occurs, translating directly into poor S/N characteristics. This is not the case for SSC scans, where shorter TR produces inherent gains in acquisition speed while maintaining a high S/N. The latter modality is only limited to the finite sampling time and bandwidth of the acquisition that can be incorporated for such repeat times.

Such as mentioned in Chapter 4, the use of SSC scans to enhance the S/N is valid when the tissues being imaged do not move during the signal acquisition. Tissue motion between RF excitations prevents the SSC regime to build the signal from transverse coherences and hence the signal characteristics are similar to those obtained for SSI scans. The strength of the signal during the approach to equilibrium is thus calculated for the SSI case since the signal from moving blood will be optimized.

Nevertheless, S/N optimization not only depends on the signal strength during the approach to equilibrium but also on the pattern of k -space data collection chosen to encode the data. The effects of k -space coverage on S/N and resolution are discussed in Section 6.2. A compromise between an optimal flip angle and the specific k -space coverage used will determine together the exact balance between the signal enhancement possible and the quality of the reconstructed images.

6.1.1 Estimation of the Signal Strength in the Approach to Equilibrium for FLASH

An estimate of the total signal strength during the approach to equilibrium for FLASH can be obtained by integrating the transverse magnetization, $M_y^+(n)$, over the number of excitations, N_{pe} , required to encode a particular phase encoding direction. Rewriting Equation 4.6

$$M_y^+(n) = M_o \sin \alpha [M_s + (1 - M_s)r^{n-1}] \quad (6.1)$$

and defining $S(\alpha, N_{pe})$ as the averaged signal strength over N_{pe} for a constant flip angle α ,

$$\begin{aligned} S(\alpha, N_{pe}) &= \sum_{n=1}^{N_{pe}} M_y^+(n) \\ &= M_o \sin \alpha \sum_{n=1}^{N_{pe}} [M_s + (1 - M_s)r^{n-1}] \end{aligned} \quad (6.2)$$

it follows

$$S(\alpha, N_{pe}) = M_o \sin \alpha \left[M_s N_{pe} + \frac{(1 - M_s)(1 - r^{N_{pe}})}{(1 - r)} \right] \quad (6.3)$$

with $M_s = (1 - E1)/(1 - r)$, $E1 = e^{-TR/T1}$ and $r = E1 \cos \alpha$. Note that two terms contribute to the strength of the signal during the approach to equilibrium. The first term represents the contribution due to steady-state conditions. The second provides the signal enhancement possible during the approach to equilibrium. Note that as $N_{pe} \rightarrow \infty$, the latter converges to a constant value, indicating that the major contribution to the signal when N_{pe} becomes large is given by the steady-state term of Eq. 6.3. The contribution of both terms can be visualized by evaluating each term independently for Equation 6.3 as is shown in Figure 6.1, demonstrating the signal variation as a function of the excitation flip angle for $N_{pe}=128$.

Note that in Figure 6.1 there is a maxima for a given number of excitations. Naming the flip angle at the maximal signal as the optimal angle α_{opt} , α_{opt} will represent the

angle at which the contribution to all the spatial frequency components of k -space will be the highest. The resulting maxima occurs at a flip angle higher than the Ernst angle, but eventually reaches the latter when the contribution of the dynamic term in the approach to equilibrium has limited contribution to the signal strength when the number of excitations is increased (the case for a 3D FLASH scan).

Figure 6.1: Signal strength for blood in FLASH with $TR=8.2$ ms and $N_{pe}=128$. The solid line represents the contribution of the steady-state and the dynamic saturation components of the approach to equilibrium. The long dashed line (Term 1) demonstrates the signal for the steady-state component while the short dashed line (Term 2), the enhancement due to the approach to equilibrium.

The contribution during the approach to equilibrium is greater when a smaller number of excitations are applied. For comparison, Figure 6.2 shows the case for $N_{pe}=64$ and $N_{pe}=128$, respectively. The optimal angle, α_{opt} is higher for $N_{pe}=64$ while the steady-state component indicates that α_{ERNST} is the same for both. This indicates

that higher flip angles can be used during the approach to equilibrium to optimize the S/N for smaller number of phase encoding steps.

The prior discussion is valid for the case of a syncopated excitation. The shape of the curves is the same but scaled accordingly to the starting longitudinal magnetization prior to the acquisition of each in-plane phase encoding step.

Slice profile effects on the signal behavior have not been considered here since for 3D imaging, a constant flip angle across each partition can be assumed.

Figure 6.2: Signal strength for blood in FLASH with $TR=8.2$ ms and $N_{pe}=128$ and $N_{pe}=64$, respectively. The solid line represents the contribution of the steady-state and the dynamic saturation components of the approach to equilibrium together. The dashed line indicates the steady state component alone. The curves have been scaled by $\sqrt{N_{pe}}$ to demonstrate signal-to-noise ratios.

6.2 The Fourier Transform, Tissue Signal and K-space Traversal

In Fourier transform NMR, the portion of k -space that majorly determines the contrast between two tissues is confined around its center, given that most of the spatial frequencies that the tissues define are concentrated around it. This suggests that the resulting image contrast obtained during the approach to equilibrium is strongly coupled to the values of the magnetization during the phase encoding of the central k -space values.

The acquisition parameters that influence the tissue contrast for data collection during the approach to equilibrium are mainly the magnetization preparation, TW , excitation flip angle, number of 3D partitions collected and the specific pattern of k -space data collection. From all parameters mentioned previously, the order in which k -space is acquired allows the greatest flexibility in contrast definition and signal optimization during the approach to equilibrium for a fixed set of parameters.

6.2.1 K-space Trajectories

There are different ordering schemes that have been proposed for collecting the data along either phase encoding direction. Each scheme has its advantages and disadvantages and the choice for either one will depend on how it affects signal-to-noise, contrast and resolution on the resulting images. Centric, sequential and cyclic k -space coverage are the k -space trajectories that are more frequently used to encode the data. Each of these trajectories is summarized in the subsequent sections. Certainly, other trajectories can be found in the literature but the ones mentioned are few of the trajectories that produce smoother transitions between phase encoding steps and were possible to implement in the imaging system used for experimentation.

Sequential Ordering

Sequential ordering has been the standard way to encode an image. This scheme acquires k -space starting from the most negative value of the phase encoding table,

$-N/2$, and linearly increases towards the most positive value, $N/2-1$ (see Figure 6.3a).

In this case, contrast between tissues relies on the signal differences after a number of RF pulses have been applied before the collection of the central Fourier lines. This indicates that the number of phase encoding steps applied before reaching the central k -space lines will greatly influence the signal and will modify the tissue contrast accordingly. In the worst case, contrast may not be the desired one if a large number of phase encoding steps are acquired, in which case, the central lines would be collected during almost steady-state conditions.

Figure 6.3: Sequential (a), asymmetric sequential (b), cyclic (c), centric (d) acquisition of k -space.

Asymmetric Sequential Acquisition

In the sequential ordering scheme, special attention must be taken in order to encode a predefined contrast if a high number of phase encoding steps is desired. A careful choice of the excitation flip angle and repetition time must be done to ensure the contrast characteristics in the reconstructed images. To partially overcome these constraints, k -space can be acquired with an asymmetric table in which the first value encoded has a desired offset, N_{off} , from the DC component, while the remaining $N - N_{off}$ lines are encoded until k -space is completely filled (see Figure 6.3b).

This approach does not have signal discontinuities in k -space like the cyclic approach does, but requires the use of partial Fourier reconstruction to eliminate Gibb's ringing.

Cyclic Ordering

In the cyclic ordering scheme, an offset number of lines, N_{off} , are collected sequentially before the central Fourier line is reached (refer to Figure 6.3c).

After the center of k -space is acquired, the phase encoding values continue to increase linearly towards the end of k -space before switching to the lower end to collect the portion that was left before reaching $-N_{off}-1$. The value of N_{off} has to be carefully chosen considering that the slightest mismatch in the signals between the first phase encoding steps collected as compared to the end ones may create intense blur and ghosting if it is close to the central Fourier line.

Centric Reordering

In the centric ordering scheme, the contrast is defined, virtually, independent of the evolution of the magnetization during the approach to equilibrium. The first line collected is the central line of k -space and subsequently, the phase encoding table toggles back and forth towards the higher values of k -space. For example, if N represents the number of phase encoding steps used, the first view acquired is 0, and then 1, -1, 2, -2... $N/2-1$ follow (Figure 6.3d).

Eddy currents are a major problem for this data collection scheme since they can potentially interfere during image reconstruction by creating major intensity variations across a uniform object. The fast eddy current components provide the strongest contribution to the signal inhomogeneity and their effect can be easily seen by observing the change in the echo location along the frequency encoding direction during the first phase encoding steps. This problem can be alleviated if a number of gradient preparation cycles are applied to stabilize the eddy currents, in the same fashion as is usually done with standard data collection during steady-state after the application of a predefined number of RF pulses. This is demonstrated in the diagram of Figure 6.4.

Figure 6.4: Eddy current and signal stabilization with the use of N gradient preparation cycles or RF/gradient preparation cycles prior to phase encoding N_{ss} steps. With the latter and centric ordering, the high k -space values are encoded first before collecting the central lines.

The gradient preparation cycles consist of a repetition of the gradient waveform

used to encode the signal without using the RF. The length of this preparatory stage will depend on how fast the eddy current effects stabilize.

The implementation of this stabilization procedure was not possible with gradient pulses alone and instead, n RF/gradient preparatory cycles, usually 7 or 15, were applied with the gradients and the RF excitation applied together before acquiring the data with centric ordering. The signal may be discarded or be included at the higher positive and negative k -space lines where the eddy current effects will affect contrast the least. This type of preparation stage has been also utilized to reduce the transient, oscillatory response of tissues with small T_1/T_2 ratio at higher flip angles (15° - 40°) in magnetization prepared acquisitions using a ROAST sequence to sample the data. This transient response is not characteristic for FLASH (see Section 4.1.1) and the latter procedure may be obviated.

The sequential and cyclic ordering schemes are less affected by eddy currents. A reverse centric ordering can be used also and for which the central Fourier line is acquired at the end of the phase encoding process. Reverse centric ordering would not have the same eddy current problems but the contrast definition advantages that centric ordering brings would be completely lost with this setup.

6.3 Filtering Effects

Non-uniformity in the signal strength of Fourier lines in k -space introduces a non-ideal point spread function (PSF) that degrades, in general, the resolution of the reconstructed images. This is the case for data collection during the approach to equilibrium.

The filtering function applied during the approach to equilibrium is not a simple one since tissues with different T_1 and T_2 values can have radically dissimilar behaviors during the transition to steady-state. This behavior will also be influenced by the type of experiment performed for which the transverse magnetization may decay or grow during the encoding of each k -space line.

The simulations presented next have been done for the approach to equilibrium for

FLASH and IR-FLASH. ROAST and IR-ROAST were not included in the evaluation for the reasons outlined in Section 4.1.2 (spoiling of the transverse magnetization due to spin motion).

6.3.1 Vessel Model

The effects that each k -space trajectory has on image resolution have been evaluated with the theoretical model depicted in Figure 6.5. This simple model includes objects of finite extension with a single tissue property, producing in the case under study, a more realistic situation in the evaluation of the approach to equilibrium effects on the resolution of pulmonary vascular structures. The properties of blood have been integrated in this model. A vector of 128 points was chosen such that the filtering functions displayed in the following sections match the experimental parameters.

Figure 6.5: Vessel resolution model. The widths in pixels of the vessels evaluated (from left to right) are: 20|10|10|5|13|21

6.3.2 Simulation parameters for FLASH and IR-FLASH

Blood has been utilized for the simulations to quantify the resolution loss for the different ordering schemes with $\rho=0.8$ and $T_1=1200$ ms. T_2^* decay along the frequency encoding has been neglected in the simulations by considering that the sampling window is considerably shorter than T_2^* of blood.

The approach to equilibrium curves were derived for FLASH selecting a repeat time of 8.2 ms and a flip angle of 9° and 14° , respectively. The corresponding approach to equilibrium curve for both angles is depicted in Figure 6.6.

Figure 6.6: Approach to Equilibrium for FLASH with $TR=8.2$ ms and 9° and 14° flip angles, respectively.

A TR of 8.2 ms and a flip angle of 10° were used for IR-FLASH. The inversion times were calculated accordingly for each ordering scheme to null out the signal for

blood at the central Fourier line assuming a single shot experiment (or $TW=\infty$ for a 3D acquisition). The choice for a 10° flip angle was made to allow for a zero crossing for blood with the sequential order acquisition.

Figure 6.7: Approach to equilibrium for IR-FLASH for different inversion times.

Table 6.1 summarizes the different inversion times used for all four k -space trajectories evaluated. Figure 6.7 demonstrates the magnetization dynamics for the three inversion times selected.

The computation of TI for IR-FLASH in the particular cases addressed was carried by evaluating Equation 4.14 with $TW=\infty$. For the asymmetric sequential and cyclic acquisitions, TI was selected for blood suppression by having the DC component of the signal collected after 31 excitations of the RF train.

k-space ordering	Inversion time (ms)	RF pulses
sequential	34	64
asymmetric sequential	510	32
cyclic	510	32
centric	832	1

Table 6.1: Inversion times calculated for blood for $TR=8.2$ ms, $\alpha=10^\circ$ and different k -space ordering schemes.

Filtering Effects with Sequential Ordering

The PSF that will affect the resolution in the reconstructed image will be very much dependent on the pattern utilized for k -space coverage. Analytic expressions for the filtering functions may be hard to find for all ordering schemes and numerical evaluation must follow.

An analytical expression can be easily obtained for the case of sequential ordering by following [43] and using Equation 4.6 to define a filtering function, $h(k)$, independent of position

$$h(k) = \begin{cases} [M_s + (1 - M_s)r^{k-1}] & \text{for } -N\Delta k \leq k \leq (N - 1)\Delta k, \\ 0 & \text{elsewhere} \end{cases} \quad (6.4)$$

where $r=E1 \cos \alpha$ and $M_s=(1 - E1)/(1 - r)$. $H(x)$, the filtering function in the data domain is derived by applying the Fourier transform on $h(k)$

$$H(x) = \int_{-K}^K M_s e^{2\pi kx} dk + \frac{1}{r} \int_{-K}^K (1 - M_s)r^k e^{2\pi kx} dk, \quad (6.5)$$

where $K=N\Delta k$. Performing the integration yields,

$$H(x) = M_s \frac{1}{\Delta x} \text{sinc}\left(\frac{\pi x}{\Delta x}\right) + \frac{1 - M_s}{r} \left[\frac{r^{\frac{1}{2}\Delta x} e^{\frac{i\pi x}{\Delta x}} - r^{-\frac{1}{2}\Delta x} e^{-\frac{i\pi x}{\Delta x}}}{\ln r + 2\pi xi} \right] \quad (6.6)$$

The pixel dimension, Δx (R_x), is defined as FOV/N with FOV, the field-of-view used in the phase encoding direction.

6.4 General Point Spread Function and Filter Evaluation

A one-dimensional discrete Fourier transform (DFT) of the vessel model was generated. The real and imaginary channels of the transformed model were then multiplied by the approach to equilibrium curves and followed by an inverse Fourier transform (IDFT) to observe the filtering effects on the vessel model. In order to apply these procedures with a more complex model involving other tissues, a separate procedure for each tissue such as described earlier must be performed, following a complex summation of all the transformed tissues weighted by their individual approach to equilibrium curves before performing the IDFT.

The real PSF convolved with the images for each of the k -space ordering schemes has been evaluated including the effects of a finite sampling window by performing a 512 point DFT and zero padding. The ideal windowing function which is shown for comparison, was also evaluated by performing a 512 point DFT over a 128 point box-car function in order to produce an interpolated version of the windowing function. The response obtained after the DFT was then multiplied by 4 and the phase encoding axis divided by 4. In the comparison, the peak of the PSF for the ideal windowing function was set to the steady state value for each set of imaging parameters evaluated.

On the other hand, the effects of the finite sampling window were eliminated from the evaluation of each k -space order over the vessel model by doing only a 128 point DFT so the filter effects of the latter were shown without the interference of Gibb's ringing.

Next, the four different k -space ordering schemes outlined in Section 6.2.1 are evaluated in Section 6.5. Only magnitude images are reconstructed for all the comparisons.

6.5 Evaluation of the Point Spread Functions

The PSF of the different k -space trajectories utilized are calculated according to the signal obtained from the sequence parameters used in Section 6.3.2 for FLASH and

IR-FLASH. The PSF are compared in all cases with the rectangular windowing PSF.

6.5.1 PSF for the FLASH simulation

Figures 6.8a-d show the resulting amplitudes changes across k -space for sequential, asymmetric sequential, cyclic and centric ordering schemes for both flip angles evaluated.

Figure 6.8: k -space weighting for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) for the approach for FLASH with $TR=8.2$ ms and flip angles of 9° and 14° , respectively.

The resultant PSF for the approach to equilibrium for FLASH can be seen in Figure 6.9 for the 14° degree flip angle case. The higher flip angle is shown here since

the variation of the magnetization over k -space is higher and the effects on the resulting PSF can be better visualized.

Figure 6.9: PSF for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) acquisition compared to the ideal PSF for the approach for FLASH with $TR=8.2$ ms and $\alpha=14^\circ$.

It is seen that the PSF for the asymmetric sequential acquisition (Figure 6.9b) is broader than that for the other k -space trajectories due to the lack of the high spatial components in one side of k -space (which have been zeroed out). This produces Gibb's ringing in the reconstruction with a spatial frequency directly associated with the frequencies that have both negative and positive components in k -space. Nevertheless,

this particular example is able to maintain the resolution of small objects but the structures will be blurred accordingly. In practice, the asymmetric sequential example fills all k -space values before reconstruction. The portion of k -space which is contained in lines $N - N_{off} \leq k \leq N$, which correspond to higher k -space values than those possible with the reconstruction, will not contribute to improve the resolution of the reconstructed image although some aliasing effects might exist.

Figures 6.10 and 6.11 demonstrate the effects of the different PSF functions on the vessel model for the 9° and the 14° flip angle cases.

Figure 6.10: Resolution effects on vessel model for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) for the approach for FLASH with $TR=8.2$ ms and $\alpha=9^\circ$. The dashed line indicates the steady-state value.

Both results are shown to demonstrate the effects of being closer to the optimal flip angle for imaging blood. It can be seen that for both flip angles, considerable gain in signal for wider structures is possible for centrically ordered data sets. It can be easily seen that to have a uniform enhancement for all vessel sizes, all values of k -space have to have the same amplitude.

Figure 6.11: Resolution effects on vessel model for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) acquisition for the approach for FLASH with $TR=8.2$ ms and $\alpha=14^\circ$. The dashed line indicates the steady-state value.

6.5.2 PSF for the IR-FLASH simulation

Figure 6.12a,b,c,d show the resulting amplitudes changes across k -space for sequential, asymmetric sequential, cyclic and centric ordering schemes for a flip angle of 10° with

the values of TI shown in Table 6.1.

The resultant PSF for IR-FLASH can be seen in Figure 6.13 and the resulting effects on the vessel model in Figure 6.14. Opposite to the case of FLASH, the amplitude of signal remaining in the vessels grows with a smaller vessel diameter.

Figure 6.12: k-space weighting for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) for the approach for IR-FLASH with $TR=8.2$ ms and flip angle $=10^\circ$.

Figure 6.13: PSF for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) acquisition compared to the ideal PSF for the approach for IR-FLASH with $TR=8.2$ ms and flip angle of 10° .

Figure 6.14: Resolution effects on vessel model for sequential (a), asymmetric sequential (b), cyclic (c) and centric (d) for the approach for IR-FLASH with $TR=8.2$ ms and a flip angle of 10° . The dashed line indicates the steady-state value.

6.5.3 Use of Higher Flip Angles with IR-FLASH

The use of lower flip angles have been emphasized to benefit the most from the approach to equilibrium. If moving tissue did not experience a FLASH like behavior in an SSC sequence, the extended approach to equilibrium for SSC could be used to maintain the contrast developed for a longer train of pulses as well as using higher flip angles to optimize for S/N. Nonetheless, the use of higher flip angles in any case can be done to enhance shorter T_1 tissues while suppressing the signal for tissues with longer T_1 values

in conjunction with the inversion pulse. In the previous section, a flip angle of 10 degrees was used to evaluate the filtering function over the vessel model. The comparison shown in Figure 6.15 intends to demonstrate the signal suppression possible with an inversion pulse on the vessel model in conjunction with the use of centric ordering at a slightly higher flip angle.

Figure 6.15: Filtering effect comparison for a centric ordered acquisition for $\alpha=10^\circ$ (a) and $\alpha=14^\circ$ (b) for IR-FLASH with $TR=8.2$ ms, $TI=832$ ms and $TW=\infty$.

The filtering function is not that much different with the higher flip angle but the fact that shorter T_1 tissues can benefit from similar or higher S/N with a flip angle which is closer to the Ernst angle as compared to the longer T_1 tissues, allows for an improved contrast.

6.6 Variable Flip Angle Imaging

In previous sections, the need for k-space ordering strategies to optimize S/N as well as a convenient choice for the excitation angle during the approach to equilibrium for a particular tissue of interest has been pointed out. During the approach to equilibrium, centric ordering was found to be the most flexible scheme to encode the signal in terms of contrast manipulation and S/N issues.

Variable flip angle imaging can be used to further optimize the S/N characteristics and filter response during the approach to equilibrium. This was first introduced by Stehling [44] with ORANGE (Optimized (incremented) RF-Angle Gradient Echo imaging) and Holsinger [45]. A flip angle series is calculated upon setting constraints over the signal response as it approaches steady-state.

In ORANGE two conditions are met. First, the transverse magnetization throughout the sequence execution must be maintained constant. Secondly, the longitudinal magnetization at the end of the acquisition is forced to be zero (the longitudinal magnetization is tipped down fully to the transverse plane with $\alpha=90^\circ$). These conditions allow the utilization of all the magnetization available for the improvement of the S/N while the filter response is ideal, constant magnetization response over k -space. Since the magnetization response is constant over all lines acquired, the different ordering schemes discussed previously in Section 6.2.1 will have no effect on S/N or resolution.

Assuming that complete spoiling of the transverse magnetization takes place prior to each excitation pulse, then:

$$M_z^-(n+1) = M_z^-(n) \cos \alpha_n E1 + M_o(1 - E1) \quad (6.7)$$

where $\cos \alpha_n$ is the flip angle of the n th pulse and $E1=e^{-TR/T_1}$. Imposing the condition of equal transverse magnetization for successive excitations, it follows that

$$M_z^-(n) \sin \alpha_n = M_z^-(n+1) \sin \alpha_{n+1} \quad (6.8)$$

Substituting Equation 6.8 into Equation 6.7 yields the following difference equation for flip angles

$$\sec \alpha_{n+1} = \frac{M_o(1 - E1)}{M_z^-(n)} \sec \alpha_n + E1 \cot \alpha_n \quad (6.9)$$

Using Equation 6.9 in conjunction with Equation 6.7 to determine the current value for $M_z^-(n)$, the correspondent flip angle series can be calculated by iteration given a starting guess value for the initial flip angle.

Figure 6.16 demonstrates a flip angle series calculated to optimize the signal from stationary blood with $TR=8$ ms and 64 and 128 RF excitation pulses. Note that the flip angle series increases monotonically until reaching the last phase encoding step. The behavior of the tail encompassing the last excitations applied is similar when N_{pe} is high but only to the point in which steady-state has not been reached or the signal gain is smaller than that for steady-state imaging at the Ernst angle.

Figure 6.16: Incremental flip angle series calculated for 64 and 128 RF excitations for blood with a FLASH sequence and $TR=8$ ms. M_y is maintained at 0.1357 for $N_{pe}=64$ and 0.105 for $N_{pe}=128$ of the maximum magnetization for all phase encoding steps. For comparison, at the Ernst angle (6.60°), $M_y=0.046$, approximately half the signal gained from the variable flip angle approach for $N_{pe}=128$.

A modification of this approach can be used to optimize S/N further when the shape of filtering function in k -space is introduced as a variable. This approach has been recently analyzed [46]. A target filtering function with a given tolerance and the signal

level for a desired tissue are selected. Furthermore, sampling bandwidth and repetition time can be included as two new variables that would allow further modifications of the signal and S/N characteristics during the approach to equilibrium.

These variable flip angle approaches and the manipulation of other imaging parameters are tissue dependent and severely distorted PSF can be introduced for tissues with relaxation parameters that substantially differ from those used for the calculation.

These concepts are of interest for pulmonary imaging since the only tissue of interest within the pulmonary system is the circulating blood. This would eliminate the compromise for having an optimal filter behavior for all the tissues. Nevertheless, blood is not stationary and signal enhancement considered in all the techniques need to include a dependence on blood flow rates. The practical implementation of the variable flip angle approach was not possible due to limitations in the imager hardware, not allowing a desired flip angle per phase encoding step to be programmed for the high number of slices (64-128) usually encoded.

6.7 k-space Ordering Effects in a Vessel Resolution Phantom

To demonstrate the effects of k -space ordering and approach to equilibrium as discussed in Section 6.3, a vessel resolution phantom was constructed. The vessel resolution phantom consisted of multiple glass tubes with different diameters such as used in the theoretical model of Section 6.3.1. Glass tubes were preferred over plastic ones since it was noted that in certain occasions, plastic tubes delivered a small signal due to the short echo times used in the experiments. The diameters of the tubes evaluated where: 27 mm, 15 mm, 10 mm, 7 mm, 5 mm and 3 mm, respectively, from left to right. The tubes were filled with a solution with an approximate $T_1=1200$ ms and $T_2=66$ ms, with a mixture such as described in Section 7.9 to mimic the relaxation characteristics of blood.

A 2D sequence using a ROAST structure with RF spoiling was utilized to acquire

the data. This setup was preferred over FLASH following experimental verification on the approach to equilibrium for several trials in which FLASH with and without RF spoiling was compared to ROAST with RF spoiling. A $TR=9$ ms was selected and the approach to equilibrium verified for a flip angle of 14° for a FLASH acquisition and 10° for IR-FLASH. Slice selection was accomplished using a 1.280 ms RF pulse in the presence of a 4 mT/m gradient. For these parameters, the slice profile is more likely to present a gaussian profile and will make the enhancement in the tubes to deviate from that obtained in the simulations in Section 6.5.

The effects of the eddy currents on the vessel phantom are demonstrated in Figure 6.17. Stabilization of eddy currents is important before data collection is initiated in order to avoid phase shifts along the frequency encoding direction during the acquisition of the central Fourier lines.

These effects are especially enhanced for the case of centric reordered data sets (see Figure 6.17d), and manifests as a smear along the direction of the phase encoding (left to right). Part of these effects can also be attributed to the interference of eddy currents during the slice selection process and signal refocusing.

Section 6.2.1 proposed the use of gradient preparatory cycles before data collection to minimize the effects of eddy currents. The inability to perform this strategy for a 3D data collection with the hardware available and use centric ordering to obtain the maximum enhancement possible upon the inclusion of TW from all the structures, gradient preparatory cycles in conjunction with the RF excitation were applied before centrally ordering the data. 7 and 15 preparation cycles (designated as “prep” cycles) were applied by filling the outer portion of k -space (higher values) first before turning the phase encoding to collect the central Fourier lines.

The results from 15 and 7 RF/gradient preparation cycles are demonstrated in Figures 6.17b and c, respectively. Note that the smearing is reduced as the number of preparation cycles is increased. For a sequential acquisition (Figure 6.17a), the smearing is virtually eliminated.

Figure 6.17: Effects of eddy currents for a centric acquisition with different number of RF/gradient preparation cycles performed before data collection. (a) sequential acquisition. (b) centric acquisition with $prep=15$. (c) centric acquisition with $prep=7$. (d) centric acquisition. 128 lines were encoded with $\alpha=14^\circ$ for all the examples.

Figure 6.18a demonstrates the same case as in Figure 6.17d but the acquisition took place after 40 gradient preparation cycles were performed. The remnant effects on the image are those caused by the filtering induced from the changing magnetization during data collection. It should be pointed out that even in theory (see Section 4.1.2), the RF spoiling techniques cannot eliminate the effects of the transverse coherences during the application of the first RF pulses and an oscillatory behavior for the magnetization will

always be present and contribute as an extra filtering term during data collection.

Figures 6.18c,d show profiles taken through the vessel resolution phantom collected with 40 gradient preparation cycles with centric ordering (Figure 6.18a) and data collected sequentially (Figure 6.18b), respectively.

Figure 6.18: Filtering effects on centric and sequential k -space collection without eddy current effects using 40 gradient preparation cycles. (a) centric acquisition, (b) sequential acquisition. (c) profile taken through (a), (d) profile taken through (d). 128 lines and 14° flip angle.

Note that the signal is higher in the case of centric ordering while the edges are smoother than those presented in the sequential acquisition. Note that the smallest feature maintains almost the same signal for both cases. Filtering effects still prevail even for the sequential acquisition mode but its effect results in the enhancement of the edges of all the objects given that the high signal values collected at the start of data collection are stored at one edge of the high portion of k -space (reflected as an increase

in the boundary definition).

Figure 6.19: Filtering effects of IR-FLASH. (a) demonstrates the case for cyclic data collection with the central k -space line collected after covering $\frac{1}{4}$ of k -space. (b) centric data collection. (c) and (d) show the profiles through the phantom shown in (a) and (b). 128 lines with a 10° flip angle readout.

The filtering effects for an IR-FLASH acquisition are demonstrated in Figures 6.19a,b for a cyclic acquisition collecting 31 points prior to the collection of the central Fourier line and centric ordering, respectively. The experimental values for TI in order to null the signal for the substance in the larger tube were 15 ms and 70 ms, respectively. The short TI only allowed for one gradient preparation cycle for the cyclic data collection, while a total of 16 preparation cycles for the centrically reordered data. In both cases, the edges of all the tubes are enhanced along the phase encoding direction due to the highpass filtering effects of the IR-FLASH acquisition when a large number of phase encoding lines are acquired.

Profiles taken across the phantom from Figures 6.19a,b are demonstrated, accordingly, in Figures 6.19c,d. Here it can be seen the dramatic effect that the filter produces on the signal intensities at the edges and signal within the tube. The signal within the tubes varies as a function of its diameter, and the degree of suppression also depends from the constructive or destructive interference between the edges. Note that for the centric acquisition (Figure 6.19b), the filtering effect not only enhances the edges but produces a smear along the phase encoding similar to the one shown in Figure 6.18a.

These observations signal the caution that must be taken during the interpretation of clinical cases in which structures with varying sizes are to be nulled out with this type of scans. On the bright side, the amplitude of the peaks still remains lower than the value at steady-state conditions.

6.8 Discussion on Resolution and Signal Enhancement with k -space Reordering

This chapter has demonstrated the effects that k -space coverage has on the image resolution and S/N using a vessel model for the evaluation. The signal enhancement and the strength of the filtering effects are factors that become interdependent when data is collected during the approach to equilibrium.

Among all the schemes evaluated, the centric ordering is the most appealing one since it permits a better control of the contrast. The definition of the signal at the first lines of k -space is also very much independent of the imaging parameters used. Nevertheless the use of centric ordering is limited to the resolution of the objects that are to be depicted in the image and the signal for a particular structure will be highly dependent on its dimensions along the phase encoding. For objects extending over the whole FOV, the signal is constrained in a small portion around the center of k -space and higher flip angles can be used to enhance or suppress the signal in this case. On the other hand, smaller objects will be suppressed at higher flip angles and the values obtained will be close to those found at equilibrium conditions, such as noted in Figure 6.11d,

affecting in this fashion the vessel represented by the width of one pixel.

For the centric ordering, the filtering function is real since it is symmetric about the center of k -space, as opposed to the sequential, sequential asymmetric and cyclic orders, where the filtering function is complex. The shape of the approach to equilibrium curve acts, in most of the cases, as a complex filter function since opposite points in k -space will have generally different signals (not symmetric about the origin of k -space). The shape of the filtering function has been previously addressed for a number of k -space ordering schemes [47, 48, 49] and has been evaluated in different regions in the body to study the effects of these novel approaches in disease discrimination.

In IR-FLASH acquisitions, the filtering function for all the different k -space sampling schemes is similar and can be interpreted as a highpass filter that contributes to enhance the tissue boundaries such as seen in Figure 6.14 and practically in Figure 6.19.

The slope of the magnetization at the time the central Fourier lines are collected can be taken as an indicative of the performance of a particular k -space sampling strategy in regards to its filtering effect on the images. To alleviate or reduce the problem of signal variation across k -space, k -space segmentation has been employed in an attempt to produce a milder filtering function on the image as well as to help achieve a more desired contrast with any ordering scheme [47]. This method requires the collection of multiple segments to cover k -space, each segment containing a fixed number of lines. The imaging time is increased by the ratio of the number of lines to fill in all the phase encoding steps required for a desired resolution and the number of lines per segment. Note that in the limit of having one line per segment, the acquisition is again the way k -space is acquired in the more standard format, in which each k -space line collected has the same intensity and filtering effects are completely eliminated. Each time the number of lines per segments is decreased, the slope through the center of k -space is reduced and consequently the finite window will be the only factor affecting the image resolution.

6.9 Summary

This Chapter has addressed the benefits from data collection during the approach to equilibrium as well as its disadvantages. Simulations were performed for a FLASH and an IR-FLASH experiment on a vessel resolution model to quantify the signal enhancement or suppression possible. The form of the filtering function introduced as a function of the pattern of k -space data collection along the phase encoding during the approach to equilibrium has been examined and experimentally confirmed on a vessel resolution phantom with vials containing a mixture with a T_1 similar to that of blood.

Chapter 7

Vascular Enhancement During the Approach To Equilibrium

Magnetic resonance angiography (MRA) has benefited from the fact that blood motion acts as the blood's own contrast agent and permits its visualization against background tissues. This Chapter demonstrates the behavior of moving blood for a continuous and a syncopated FLASH experiment, and quantifies the degree of enhancement possible for each case in relation to the pattern of k -space data collection used. A theoretical treatment as well as experimental data is presented on a flow phantom and on human volunteers. The results presented should be closely related to Chapter 6 given that the degree of enhancement possible with a syncopated excitation will depend strictly on the pattern of k -space chosen for data collection.

7.1 Signal Characteristics for Flowing Material in a Continuous Excitation

Considering pluglike flow through a vessel perpendicular to the excited volume with a constant velocity V_f , the number of RF excitation pulses, N_{RF} , that a single spin experiences at some location d from the edge of the volume is determined by

$$N_{RF} = \text{integer part of } \left(\frac{d}{V_f T_R} \right) \quad (7.1)$$

where TR is the interpulse interval. The signal along the vessel due to inflow of freshly magnetized spins as seen from the edge of the volume follows the same behavior as the approach to equilibrium curve for FLASH for a stationary tissue as it evolves towards equilibrium conditions. Therefore, Equation 4.6 also represents the expression for the signal behavior for a standard TOF that does not include any recovery period, such as introduced for the case of a syncopated FLASH excitation in Section 4.3.1. Therefore, the signal along the vessel is determined by

$$M_y^+(N) = M_o \sin \alpha [M_s + (1 - M_s)r^{N-1}] \quad (7.2)$$

where $E1 = e^{-TR/T_1}$, $r = E1 \cos \alpha$ and $M_s = (1 - E1)/(1 - r)$. The signal at position d is calculated by setting $N = N_{RF}$ according to Equation 7.1.

Since the behavior follows the approach to equilibrium for FLASH, an analogy on the behavior of the signal for flowing tissues can be made with the approach to equilibrium curves of Figures 4.1 and 4.2. These figures demonstrate the effects of two different repeat times and flip angles on the approach to equilibrium. It can be seen from what is implied by Equation 7.1 that the enhancement curve for blood for a different set of experiments is preserved as long as the product $V_f TR$ is maintained constant between experiments. The enhancement along the vessel due to inflow for a fixed flow velocity will be more extensive as longer repeat times are chosen, and viceversa, if flowing spins present higher velocities the same situation will be displayed as a result of a reduction of the number of RF pulses seen by the flowing spins. Nevertheless, the contrast between the flowing spins and surrounding stationary material will be greater for higher flow velocities. The opposite situation arises when lower flow velocities and shorter repeat times are used, resulting in a reduced enhancement due to flow along the vessel. A parallel behavior is only seen for changes in the excitation flip angle. Higher flip angles produce faster saturation of the spins as compared to lower flip angles, translating into

an overall shortening of the enhancement possible for flowing spins.

If a spin is subjected to a finite number of excitations, its signal can be optimized at d by choosing an optimal flip angle. This is depicted in the plot of Figure 7.1 which demonstrates the signal for a FLASH experiment as it varies with flip angle for blood spins experience an increasing number of RF excitations as they travel along a vessel. As the number of excitations experienced grows towards infinity, the optimal signal enhancement approaches the optimal flip angle for FLASH during steady-state conditions, expressed by the Ernst angle with $\alpha_{ERNST} = \cos^{-1}(E1)$.

Figure 7.1: Signal versus flip angle for blood for a FLASH sequence with $TR=8$ ms for different values of N_{RF} . As N_{RF} increases for a flowing spin at location d , the angle for optimal signal approaches that of a FLASH sequence at steady-state conditions ($T_{blood}=1200$ ms).

7.2 Enhancement of Flowing Material with a Syncopated FLASH Excitation

During a continuous excitation, the signal for tissue remaining within the imaged slab during the whole data acquisition would not change after equilibrium is reached. The signal from inflowing spins changes along the vessel length but spins become quickly saturated downstream when short TR 's are used.

Recalling the syncopated FLASH structure introduced in Section 4.3.1, the choice of a non-zero wait time TW allows stationary tissues to recover partially their longitudinal magnetization and follow the signal predicted by Equation 4.12 when the spin are first excited, or Equation 4.13 during equilibrium conditions.

For moving spins, such as blood, the situation is slightly different. For some spins, TW represents the time for which saturated blood can be replaced by fully magnetized blood moving into the imaging volume as if it were a stationary tissue and $TW=\infty$ was chosen. For this condition, the signal enhancement, S_E , between a syncopated and a continuous RF excitation at position $d \leq V_f TW$, is given by

Case 1:

$$S_E = \frac{S_{TW \neq 0}}{S_{TW=0}} = \frac{M_o \sin \alpha}{M_y^+(N_{RF})} \quad (7.3)$$

where N_{RF} and $M_y^+(N_{RF})$ are evaluated using Equations 7.1 and 7.2, respectively. For a spin at position $d \geq V_f TW$, S_E will be given by

Case 2:

$$S_E = \frac{M_y^+(p) \cos \alpha ETW + M_o(1 - ETW) \sin \alpha}{M_y^+(N_{RF})} \quad (7.4)$$

with $p = \text{integer part of } (\frac{d - V_f TW}{V_f TR})$ and $ETW = e^{-TW/T_1}$.

The regions defined by the previous cases have been denoted as the TW and the saturation regions. The last case to consider is the one in which a spin at position d has seen multiple recovery periods (i.e., spins stay inside the imaging volume for a long period of time). For a distance $d=V_f(N_s TR + TW)$, S_E is given by

Case 3:

$$S_E = \frac{M_y^+(k, t)}{M_y^+(N_{RF})} \quad (7.5)$$

with $k = \text{integer part of } (\frac{N_s TR + TW}{N_s TR})$ and $t = (\frac{d}{V_f TR}) - k N_s$, N_s is the number of RF excitations per RF string and $M_y^+(k, t)$ is the signal for a stationary spin approaching equilibrium as described by Equation 4.12. Figure 4.6 is a pertinent example. This condition is likely to be seen in an experimental setup using low flip angles, short TW , centric reordering and a small number of excitations applied per RF string, in which case the signal along a vessel should have a staircase appearance.

The three conditions previously described provide the signal for the instance right after TW and the first RF pulse of the next string of RF pulses before the system experiences the remaining excitations. The first two cases are represented in Figure 7.2b, demonstrating the TW region and the saturation region. These can be compared with the situation for the more standard time-of-flight (TOF) enhancement as shown in Figure 7.2a. The gray levels demonstrate the degree of spin saturation, with the darker levels indicating more saturation.

The signal behavior for those spins appearing after the region of complete refreshment follow the enhancement curve for a standard TOF experiment (including the uniform recovery of the longitudinal magnetization for all spins during TW).

In reality, to complete all the phase encodings steps necessary to form the image in a desired direction, RF excitations must follow and spin saturation will occur, driving the whole ensemble of spins to approach the usual equilibrium for stationary tissue at the rate characteristic for the flip angle and TR used.

Figure 7.2: Diagram of the enhancement behavior in a vessel with plug flow for a syncopated excitation with an ideal RF profile. The first line demonstrates the case for a TOF sequence (a). After TW , fresh spins with velocity V_f fill region D_{TW} and previous excited spins recover some longitudinal magnetization (b). Three regions start developing after several excitations, namely, an inflow region, a TW region and a saturation region (c,d). After a high number of excitations are applied, the system reaches equilibrium and the effects of TW disappear, the enhancement being equivalent to that of a TOF sequence (e). The gray levels indicate the degree of spin saturation (the darker the region the more saturated the spins).

Assuming an ideal excitation profile across the imaging volume and considering the first two cases outlined, the enhancement due to the introduction of TW can be

easily summarized. For those spins that are refreshed during TW , the signal evolves from maximum magnetization and will follow the approach to equilibrium in subsequent excitations. At the same time that this occurs, fresh magnetized blood from the inflowing end will enhance as if it were a normal TOF experiment and displace those spins that entered during TW , as seen in Figures 7.2c,d. Finally, after a large number of excitations, the effects of TW are consumed and the whole system ends up as in the case of a standard TOF sequence, as seen in Figure 7.2e.

Figure 7.3: Signal behavior for blood for phase encoding steps $N=1$, $N=8$, $N=16$, $N=64$ and $N=128$ for a syncopated FLASH excitation using $TW=500$ ms and $TR=8$ ms in the presence on an ideal profile with $\alpha=14^\circ$.

Figure 7.3 demonstrates the evolution of the magnetization for several values of k -space, analog to the situation demonstrated in the diagram of Figure 7.2. Note that there are discontinuities in the behavior due to the differences in the longitudinal magnetization of the spins remaining inside the volume as compared to those spins

refreshed during TW .

Section 7.3 focuses on the simulation of this situation for a variety of slice profiles, showing for all the behavior of the magnetization signal as it evolves during the collection of all the phase encoding steps. The results on the flow phantom in the experimental section will demonstrate these events by centrically reordering the data so that a particular line along the approach to equilibrium for the system is sampled.

7.3 Flow Enhancement in the Presence of Realistic RF profiles

In the presence of an ideal RF profile, the signal for blood spins moving at a constant velocity along a vessel obey Equation 7.2 for a continuous RF excitation or Equations 7.3 to 7.5 for a syncopated FLASH excitation. In practice, however, the RF profiles used are not ideal and do not excite portions of the volume with the same flip angle. This indicates that moving spins will experience different flip angles along their path from the edge of the imaging volume.

The effect of an imperfect slice profile can be easily visualized for a TOF experiment. In this case, the system can be treated as being only spatially dependent and the signal can be found by having Equation 7.1 define the number of excitations, $N=N_{RF}$, seen by a flowing spin and a flip angle dependent function, $\alpha(N)$, defining the excitation angle at some position inside the volume followed by the evaluation of Equation 7.2.

The inclusion of TW makes the matter slightly more complicated. With TW , the approach previously mentioned cannot be implemented as easily since TW introduces a transient behavior and also a temporal variable to the enhancement calculation. To account for the profile imperfection on the enhancement along the vessel, for example, Equation 4.12 must include a flip angle dependent function with the position of the spin from the edge of the imaging volume at a particular instance in time. The simulations are explored for three different profiles: a gaussian profile, a ramped profile and a

trapezoidal profile, all collinear with the direction of flow.

7.3.1 Gaussian Profile

Given a gaussian excitation profile, such as seen in Figure 7.4a, $\alpha(N)$ will be defined at a particular position within the imaging volume as

$$\alpha(N) = A_{max} e^{\frac{-d^2}{2\sigma^2}} H(N) \quad (7.6)$$

$$d = (N - V_f \cdot TR - \frac{D}{2}) \quad (7.7)$$

with A_{max} the maximum amplitude of the profile, D the thickness of the excited region with σ modulating the broadening of the gaussian and d indicating the distance from the inflowing site during the occurrence of the n th RF excitation. The function $H(N)$, a Hanning window, defined by

$$H(N) = \frac{1}{2} [1 - \cos(\frac{2\pi N}{N_{prof}})] \quad (7.8)$$

confines the extent of the gaussian profile to the desired thickness of the excitation slab so that the excitation profile tails off to zero. The variable N_{prof} is determined by calculating the number of RF excitations that a flowing spin with velocity V_f would take to cross the excitation region D for the chosen TR ($N_{prof} = D / (TR \cdot V_f)$). For high values of σ , the shape of the gaussian will be completely dominated by the Hanning window function.

Figure 7.4b reflects the effect of the gaussian excitation on the signal of blood as it evolves during the approach to equilibrium for the syncopated FLASH scan with $TR=8$ ms, 14° flip angle and $N=128$. Compared to the case of a constant RF profile, all flowing spins remaining inside the imaging volume during the 128 RF excitations never reach equilibrium.

Figure 7.4: (a) Gaussian profile apodized with a Hanning window with a maximum of 14° flip angle at the center of the profile. (b) signal behavior for blood moving at $V_f=12.5$ cm/sec for phase encoding steps $N=1$, $N=8$, $N=16$, $N=64$ and $N=128$ for a syncompated FLASH excitation using $TW=500$ ms and $TR=8$ ms.

7.3.2 Trapezoidal Profile

This flip angle distribution has been found to fit better the actual excitation profile utilized for the experimental setup. The analysis here is done for two trapezoidal profiles where the shape of the profile is defined by the variable a , defining the ratio between the plateau region to the size of the excitation region. The profile is then given by

$$\alpha(N) = \begin{cases} \frac{2A_{max}NV_fTR}{D(1-a)} & \text{for } 0 \leq N \leq \text{integer part of } (1-a)\frac{N_{prof}}{2}, \\ A_{max} & \text{for integer part of } (1-a)\frac{N_{prof}}{2} \leq N \leq N_{prof} - \text{integer part of } (1-a)\frac{N_{prof}}{2}, \\ \frac{2A_{max}[-NV_fTR+D]}{D(2-a)} & \text{for } N_{prof} - \text{integer part of } (1-a)\frac{N_{prof}}{2} \leq N \leq N_{prof} \end{cases} \quad (7.9)$$

where N_{prof} indicates the number of RF pulses needed for a spin to cross the excitation volume D and $a < 1$. Figures 7.5a,c demonstrate the trapezoidal profiles used with $a=0.6$ and $a=0.9$, respectively. To smooth the profile at the sharp transition between the ramp

and the plateau, a running average with a selectable number of points was performed over the profile (20 points were used for the examples shown).

Figure 7.5: (a) Representative shape of a real RF profile. This shape was found to match closely the profile generated with an RF excitation of $640\mu\text{sec}$ in the presence of a 2 mT/m gradient defining a 20 cm thick slab, (b) demonstrates the blood behavior for the profile shown in (a) for $N=1$, $N=8$, $N=16$, $N=64$ and $N=128$ for $V_f=12.5$ cm and FLASH with $TR=8$ ms, $TW=500$ ms. (c) Profile similar to one generated for an RF excitation of $1024\mu\text{sec}$ in the presence of a 3 mT/m gradient defining a 20 cm thick slab, (d) corresponding enhancement behavior.

7.3.3 Ramped Profile

The same situation can be defined in the case of a ramp RF function such as depicted in Figure 7.6a. The RF profile is designed so that a linear increase of the flip angle occurs across the volume of interest from the site of inflow to the volume to the outflow site. Defining α_1 , as the angle at the inflow site and α_2 , the angle at the outflow end, the Equation for the ramp is defined as,

$$\alpha(N) = \frac{(\alpha_2 - \alpha_1)N V_f TR}{D} + \alpha_1 \quad (7.10)$$

Figures 7.6a,b demonstrate a ramped RF profile and the corresponding enhancement, respectively.

Figure 7.6: Ramped RF profile with $\alpha_1=10^\circ$ and $\alpha_2=14^\circ$. (b) Corresponding enhancement for a syncopated FLASH with $TW=500$ ms, $TR=8$ ms and $V_f=12.5$ cm/sec for $N=1$, $N=8$, $N=16$, $N=64$ and $N=128$

The slope of the ramp as well as other excitation profiles can be optimized in the same fashion as referred in Section 6.6 with a variable flip angle approach. This experiment would allow for a standard TOF experiment to produce a uniform enhancement along the vessel. Taking the variable flip angle example shown in Figure 6.16, if the waveforms calculated for 64 and 128 excitations are used as the excitation profiles, the signal

enhancement will be uniform up to the point where the flip angle series is valid (assuming a straight vessel). The extent of the enhancement will depend on TR and the flow velocities involved since these are the variables that indicate the number of RF pulses a flowing spin will experience. A similar idea has been recently implemented with optimized RF pulses referred to as TONE pulses (Tilted Optimized Excitation) [50].

7.3.4 Size of the Discontinuities during the Approach to Equilibrium

Right after TW and before the next string of RF pulses excites the system, a minimum of two groups of spins are always present in which the magnetization behavior is defined by the first two cases described in Section 7.2. As the new set of RF pulses are applied, these groups of spins start approaching equilibrium and move downstream while new incoming spins replace their positions. Even though the spins in all the regions approach equilibrium at the same rate for an ideal profile, there are clear differences in the signal of each group since the starting longitudinal magnetization for each is different. For an ideal excitation profile the size of the discontinuities and their existence dies off as the number of excitations increases, blending the enhancement curve of the syncopated experiment with the enhancement of a standard TOF sequence. As the RF profile departs from the ideal case, the size of the discontinuities grows to a maximum and is reduced as the spins approach the equilibrium condition. In the case of the gaussian profile, the discontinuities are the greatest as a result of the variability of the flip angle seen by a spin as compared to other profiles. The time of appearance of the maximum discontinuity is also shifted for less ideal profiles and occurs towards the higher excitations numbers.

7.3.5 Blood Enhancement for a Parabolic Velocity Profile

The previous simulations have considered blood flow with a plug velocity profile. For this profile, the signal enhancement throughout the vessel becomes independent of the vessel radius. Practically, blood flow in vessels can be regarded as being laminar, with a parabolic velocity distribution [51] given by

$$V_f = V_m \left(1 - \frac{r^2}{R^2}\right) \quad (7.11)$$

where V_m represents the maximum velocity along the center of the vessel and R the vessel radius.

With a parabolic velocity distribution the signal enhancement is expected to be also parabolic in principle. The blood velocity close to the vessel wall is nearly zero and it can be regarded as stationary. In this case, the blood is not refreshed during TR and will tend to remain saturated during the length of the imaging experiment. On the other hand, the spins with maximum velocity in the center of the vessel get refreshed at a faster rate and saturation occurs further downstream. A similar parabolic enhancement occurs when TW is included. Nevertheless, regions which are close to the inflow site that have slow flow, will also have the chance to get refreshed during TW and have the same signal as faster spins close to the inflow site. The overall enhancement after this region will then tend to be an elongated version of the enhancement generated during a continuous excitation (i.e., the parabolic nature becomes more apparent further downstream).

7.4 Signal Behavior for Different Wait Times and Flow Velocities

The enhancement behavior of a syncopated excitation has been analyzed for a range of wait times and velocities such as depicted in Figures 7.7 and 7.8, respectively.

Figure 7.7: Influence of TW on the inflow enhancement for a syncopated FLASH excitation with $TR=8$ ms, $V_f=12.5$ cm/sec for $N=1$, $N=8$, $N=16$ and $N=128$ in the presence of a trapezoidal profile with $a=0.9$ with a 20 point running average. (a) $TW=100$ ms, (b) $TW=300$ ms, (c) $TW=500$ ms, (d) $TW=800$ ms.

For all phase encoding steps during the approach to equilibrium, the signal is always higher than the value at steady-state, which represents the case for a continuous RF excitation. This holds true for all velocities, but the signal for a continuous excitation

will tend to approach that of $N=1$ with a syncopated excitation asymptotically in the limit of very high velocities or long TR , in which case, the number of pulses seen by a flowing spin will be smaller as it travels throughout the volume.

Figure 7.8: Influence of V_f on the inflow enhancement for a syncopated FLASH excitation with $TR=8$ ms and $TW=500$ ms for $N=1$, $N=8$, $N=16$ and $N=128$ in the presence of a trapezoidal profile with $a=0.85$ (no averaging done). (a) $V_f=7.25$ cm/sec, (b) $V_f=12.5$ cm/sec, (c) $V_f=25$ cm/sec (d) $V_f=37.5$ cm/sec

For those flow velocities in which complete spin replacement occurs during TW (see Figure 7.8d), the number of excitations that it takes to approach the steady-state response is smaller since the replacement of fresh spins overrides those locations for which the spins are still approaching equilibrium. The simulation for each of the flow

velocities did not consider the averaging done over the excitation profiles performed in earlier simulations due to the change in the profile for a fixed length of the averaging filter (the excitation profile is naturally defined with less samples for higher flow velocities). To use the same averaging filter, interpolation using multiple shifted profiles must be used to recreate the sampling density for the slowest flow velocity simulated so that the effective number of RF excitations to cross the volume remains unchanged.

7.5 Flow Phantom

7.5.1 Phantom Setup and Measurements

Flow Phantom

The straight portion of a phantom developed to assess circulation patterns in the carotid arteries (Cleveland Clinic Foundation, Cleveland, OH) was used for signal enhancement quantification for experiments in which flowing signal was compared for several parameters of the syncopated acquisition. The flow phantom setup can be seen in Figure 7.9.

Figure 7.9: Flow phantom setup.

The fluid circulating in the phantom was chosen with similar relaxation properties as blood in order to have a basis for comparison with the results later shown in Section 7.6 and Section 10.3.2. The fluid consisted of a mixture of 22 mg of $MnCl_2 \cdot 4H_2O$ dissolved in 1ml arquad 10.1N solution per liter of demineralized H_2O . This solution gave initially T_1 and T_2 values of 1400 ms and 240 ms respectively in October 1990. At the time of experimentation in February 1991, the substance underwent minor changes for the T_1 relaxation and gave the measured values of $T_1=1200 \pm 66$ ms and $T_2=66 \pm 3$ ms with a standard multiecho SE sequence after evaluation with an online parameter calculation software residing in the system.

Sequence Setup

An axial excite, coronal readout sequence (axis definitions of Figure 10.1a and the sequence diagram of Figure 10.2a) was used for all the measurements. Figure 7.9 summarizes the imaging sequence setup and orientations used for all the experiments.

The syncopated FLASH scan was evaluated using $TR=8$ ms and $TE=2.8$ ms with $N_z N_x=64 \times 128$ interpolated to a 128×128 matrix and 128 partitions ($N_y=128$) defining 1.5 mm thin slices encoded coronally. This setup is similar to the one described in Section 10 for the volunteer and patient studies.

A 200 mm FOV in-plane was selected for an effective resolution of $R_x=1.56$ mm by $R_y=3.12$ mm. The short echo time was achieved by sampling the echo asymmetrically within the sampling window with 25 points before the echo. A readout bandwidth of 122 Hz/pixel, corresponding to a sampling rate of 32 μ sec, was used to collect the 128 points along the frequency encoding direction.

Two RF excitations were utilized to define a 200 mm excitation region with approximate rectangular and trapezoidal shapes using a 1280 μ sec RF pulse applied during a 3 mT/m and a 1 mT/m slice selective gradient pulse, respectively (RF bandwidth of 25.5 KHz and 8.5 KHz). The random RF spoiling option was utilized [33].

Given that the comparisons are performed for constant velocity flow, an estimate of

the flow velocity was done by using a bolus tracking technique based on a 2D FLASH sequence with a tagging pulse located upstream and oriented perpendicular to the flow direction. The tagging pulse used a flip angle of 120° and was sampled after a delay of 200 ms. The distance travelled by the tagged region was then divided by the sample delay to provide the average velocity. The length of the tubing from the pump output to the measuring site was long enough to assume that a parabolic velocity profile was fully developed. This was confirmed using the phase image of a standard SE sequence.

Measurement Protocol

Several experiments were selected to compare the enhancement patterns for the syncopated FLASH and the TOF sequence with the same imaging parameters (same sequence as the syncopated acquisition but setting $TW=0$ ms). These experiments included changes in TW , flip angle and RF profile, k -space acquisition order and evaluation during flowing and stationary conditions. Fluid velocity in the phantom was calibrated at 12.5 cm/sec with the bolus tracking technique described earlier. For all the cases evaluated the receiver settings were the same.

Centric and sequential ordering were utilized to verify the enhancement pattern as a function of k -space line collected, such as demonstrated earlier in the simulations of Section 7.2 and Section 7.3. Flip angles of 9° and 14° were explored for the comparison. Centric data collection was utilized to verify the evolution of the enhancement after the introduction of TW since this ordering scheme makes it possible to capture, virtually, the signal for each phase encoding step. The RF/gradient preparation cycles were included as outlined in Section 6.2.1. The enhancement was evaluated for $N=1$, $N=8$, $N=16$ with centric ordering, while for $N=32$ and $N=64$, sequential order was used. The relation between the diameter of the tube (2.54 cms ID) and the FOV in the slice select phase encoding direction (19.2 cms) was found appropriate to consider the correctness of the previous affirmation on the signal captured (refer to the filtering effects on the vessel resolution model discussed in Section 6.5 for which the 20 pixel

wide vial in a FOV of 128 points compare to the tube diameter and the FOV in the slice select direction utilized). The same comment can be applied as well for the sequential case. For each of the centric ordered cases examined, the indexes C_0 , C_8 and C_{16} were utilized, respectively, where the index is indicative of the number of RF/gradient preparation cycles performed before data acquisition proceeds with centric ordering. For a sequential acquisition the central line is collected after half the phase encoding steps are acquired, as usual, and denoted as sequential in all the plots.

7.5.2 Experimental Results on the Flow Phantom

Evaluation

The results shown here have been evaluated by collecting 23 uniformly distributed samples along the length of the excited portion of the tube. A ROI of 3x3 pixels (4.7 mm x 4.7 mm) was used in the evaluation to improve the S/N statistics of each sample. This makes the ROI to include a range of velocities spanning from $0.88 V_m$ to V_m due to the parabolic velocity profile.

Figure 7.10: Flow enhancement for syncopated FLASH with $TR=8$ ms and $V_f=12.5$ cm/sec. (a) $\alpha=9^\circ/TW=0$ ms, (b) $\alpha=9^\circ/TW=500$ ms, (c) $\alpha=14^\circ/TW=0$ ms, (d) $\alpha=14^\circ/TW=500$ ms.

The Effects of TW

Figure 7.10 demonstrates the signal enhancement for a syncopated FLASH experiment evaluated for $TW=0$ ms and $TW=500$ ms for a flip angle of 9° and 14° , respectively.

The results are plotted in Figure 7.11. It is worth pointing out again that the enhancement curve for a continuous excitation is in fact the approach to equilibrium behavior for the fluid in question (taking into account that a non-ideal profile is evaluated). This can be considered, indeed, an elegant setup for examining the approach to equilibrium curve for any tissue owing that for short TR FLASH sequences where TR is usually much shorter than T_2 , it is difficult to destroy transverse coherences even with the use of RF spoiling techniques, making it difficult to follow the approach to equilibrium curve for a stationary tissue (see Figure 4.3). Motion helps randomize the transverse magnetization optimally (see Section 4.1.2).

Figure 7.11: Enhancement for syncopated FLASH with $TR=8$ ms, 9° and 14° flip angles and $V_f=12.5$ cm/sec using a $TW=500$ ms and $TW=0$ ms. A higher steady-state value is found for 9° since this angle is closer to α_{ERNST} .

Such as predicted in Section 7.4 (see Figure 7.7), the degree of enhancement along the tube is directly related to the flow velocity and TW chosen, leaving for a fixed

V_f , a proportional increase in the uniformity of the enhancement with longer TW . These effects are demonstrated in Figure 7.12 and the corresponding profiles plotted in Figure 7.13. The data was collected in this case with centric ordering and 7 RF/gradient preparation pulses, or C_8 .

Figure 7.12: Flow enhancement for $TW=0$ ms (a), $TW=100$ ms (b), $TW=200$ ms (c), $TW=300$ ms (d), $TW=500$ ms (e) and $TW=800$ ms (f) for a $V_f=12.5$ cm/sec, $TR=8$ ms, $\alpha=14^\circ$ and C_8 . For longer TW , the effect of the longitudinal recovery is clearly seen since the signal is above that for a continuous excitation.

The response for C_8 data collection for those spins refreshed during TW is considerably flat in this case, and verifies the signal enhancement occurring from the site of inflow up to a distance $D=V_fTW$. Note that the slope of the curve after the inflow region indicates that longitudinal magnetization regrowth occurs for those spins for increasing values of TW , tending to equalize the longitudinal magnetization in the otherwise, saturated region. This is in accordance with the predictions of Figure 7.7 (see Equation 7.4).

Signal Behavior and Dependence on K-space Data Collection Order

The results from the experiment that verifies the resulting signal for several phase encoding steps can be seen in Figures 7.14a,b for 64 and 128 phase encoding steps and a fixed $TW=500$ ms. The phase encoding steps 1, 8 and 16 were evaluated by having the corresponding number of RF preparations cycles and centric ordering performed.

K-space lines 32 and 64 were collected sequentially instead.

Figure 7.13: Enhancement profiles for varying TW in a syncopated FLASH acquisition. The profiles demonstrated are for $TW=0, 100, 300, 500$ and 800 ms, respectively with $V_f=12.5$ cm/sec, $TR=8$ ms, $\alpha=14^\circ$ and C_8 .

The effects of the continuous inflow and disappearance of the signal gained during TW as it approaches equilibrium can be clearly seen near the inflow end as the number of RF pulses progresses during the collection of the curves for C_0, C_8, C_{16} and the other higher k -space lines encoded (compare with Figure 7.3). This also confirms that differences in signal can be readily appreciated between the phase encoding lines sampled and demonstrates the usefulness of centrally reordered acquisitions in providing the contrast seen at the time the central Fourier line is acquired.

A Less Ideal Excitation Profile

The enhancement pattern for the more realistic profile used in most human experiments is shown in Figure 7.15 for $TW=500$ ms. This compares with the simulations of

Figures 7.5b,d. Note that for the sequential data collection, a discontinuity is expected from what is seen in Figure 7.5. This is not seen in Figure 7.15, possibly as a result of the phase encoding process, the discrete evaluation of the profile along the tube as well as the size of the ROI utilized to improve S/N. Flattening of the profile is noted for the data collected with C_8 as compared to C_0 , in agreement with the simulation results of Figure 7.5b.

Figure 7.14: Evolution of the enhancement created by the introduction of TW during the phase encoding process. (a) and (b) show the resulting signal intensities for k -space lines 1, 8, 16 and 32 and 1, 8, 16, and 64 (top to bottom) for the syncopated FLASH experiment collecting 64 and 128 partitions, respectively. The profiles in (c) and (d) correspond to the data shown in (a) and (b). TW was 500 ms and $TR=8$ ms with a flip angle of 14° .

Figure 7.15: Flow enhancement in the presence of a more realistic profile for a synco-pated FLASH acquired with $TW=500$ ms, $TR=8$ ms and $\alpha=14^\circ$.

Effects of Multiple Acquisitions with Pulsatile Flow

Pulsatile flow was evaluated to verify the effects of signal averaging with multiple acquisitions. Figure 7.16a depicts the pulsatile waveform that was possible to generate with the flow phantom at the measurement site. Despite the fact that the pulsatile behavior was not adequate to simulate the pulsatile waveform in the aorta or pulmonary artery, the pulsatile effects can be readily seen on the profiles of Figures 7.16b-d, demonstrating the effect of multiple acquisitions for $N_{acq}=1-3$, respectively. The profiles demonstrated were taken along the inflow and outflow lines for comparison as it was noted that for the outflow line, the compliance effects of the tubing used already have attenuated the pulsation amplitude significantly. As expected, the averaging reduces the

non-uniformities introduced by the pulsatile flow as the number of averages increase, as a result of a more uniform coverage of k -space. In this experiment it is interesting to note from Figures 7.16b-d that the enhancement seen in previous sections with constant flow with the syncopated FLASH sequence is not seen along the inflow line after having induced the pulsatile waveform. Surprisingly, the enhancement expected for constant flow having introduced TW is demonstrated along the outflow stage instead, where the pulsatile nature of the flow has been considerably reduced. Also note, for comparison, that the signal at the edges of the slice for both the inflow and the outflow stages is the same, but the enhancement due to TW is only seen in the latter.

The pulsatile waveform was measured with a projective technique, sampling the signal with a short TR 2D FLASH sequence with velocity compensation along the slice select and frequency encoding axis, and the in-plane phase encoding gradient removed. A $TR/TE=22/10$ ms, 3 mm slice thickness and $\alpha=50^\circ$ were the imaging parameters used in this case. After an IDFT was performed only along the frequency encoding direction, the intensity variation due to the changing inflow could be directly related to the pulsatile waveform induced. The signal variation recorded, such as seen in Figure 7.16a, was small due to a bad choice of the imaging parameters for the pulsatile waveform expected with a maximum flow velocity of 33 cm/sec. The pulsatile waveform should have been recorded with a higher flip angle, i.e. 90° , and a thicker slice, i.e. 1 cm, to have a higher sensitivity to inflow effects. According to this measurement, the period of the waveform was ~ 750 ms.

Figure 7.16: Effects of averaging multiple acquisitions for a pulsatile waveform. (a) shows the pulsatile waveform recorded at the measurement site on the inflow tube. (b), (c) and (d) show the effects of $N_{acq}=1-3$, respectively. The profiles are plotted such that the inflow occurs from right to left. The amplitude variations in the inflow line (solid line) are reduced as the number of acquisitions is increased. Note that the outflow waveform (dotted line) remains fairly constant despite the averaging indicating that the compliance of the tube has already attenuated the pulsatile waveform to a degree that flow has a constant velocity. Imaging parameters: syncopated 3D FLASH, $TR=8$ ms, $TW=500$ ms, $TE=2.8$ ms, $\alpha=14^\circ$, $N_y=64$, $N_z N_x=64 \times 128$, $R_x=1.56$ mm, $R_z=3.12$ mm, $R_y=3.0$ mm and C_3 .

7.6 Studies in the Region of the Carotid Arteries

7.6.1 Methodology

The sequence setup and experiments realized on the flow phantom were repeated in the region of the carotid arteries of several volunteers in order to demonstrate the effects of TW as well as the influence of centric and sequential k -space data collection for the syncopated FLASH acquisition. The region of the carotids was selected for the comparison owing to the similar geometry used for the flow phantom as well as ease of evaluation. The study was performed using the body coil for RF excitation in order to produce a homogeneous excitation over the region of interest while a Helmholtz pair placed over the neck was utilized for signal reception. The Helmholtz pair does not provide a homogeneous reception across the entire FOV and the resulting enhancement profiles do not behave like those displayed in the previous section in some respects given that for the flow phantom the body coil sensitivity was uniform across the FOV. This is irrelevant for the comparison since coil sensitivity does not change between experiments and it is the ratio between signals which is the important parameter.

7.6.2 Signal Behavior and Dependence on K-space Data Collection Order

Figures 7.17a-f demonstrate 2 cm MIPs in a frontal projection generated from the coronally acquired slices on the neck of a healthy volunteer. The signal enhancement for blood along the left carotid distribution of all the cases demonstrated in Figure 7.17 is analyzed in the plot shown in Figure 7.18. The left carotid artery was evaluated since it departs directly from the aortic arch as opposed to the right carotid artery. The data has been plotted taking a $3.2 \times 3.2 \text{ mm}^2$ region every centimeter, up to the region of the carotid bifurcation. The behavior of the muscle and fat signals surrounding the carotid artery were evaluated at the center of the FOV and the values obtained from the data are listed in Table 7.1 for all the combinations performed. Note from Table 7.1 that the fat signal experiences very little change in intensity.

Figure 7.17: Enhancement pattern in the carotid arteries of a healthy volunteer. (a) and (b) show 2 cm coronal MIPs acquired with $TW=0$ ms, for $TR=8$ ms and $TR=12$ ms, respectively. (c),(d), (e) and (f) were acquired using a $TW=500$ ms with $TR=8$ ms and C_0 , C_8 , C_{16} and sequential acquisitions, respectively. All examples were collected with a syncopated FLASH 3D, $TE=2.8$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x:N_z=64 \times 256$, $R_x=1.05$ mm, $R_y=1.5$ mm, $R_z=3.15$ mm and $N_{acq}=3$.

Figure 7.18: Profile taken along the left carotid artery comparing the effects of k -space ordering during data collection. The data sets compared are: C_0 / $TW=500$ ms, C_8 / $TW=500$ ms, C_{16} / $TW=500$ ms, sequential with $TW=500$ ms and sequential with $TW=0$ ms for $TR=8$ ms and $TR=12$ ms. The points for the plot are taken every 1 cm along the vessel.

k -space ordering	TW (ms)	TR (ms)	flip angle	Fat	Muscle
centric C_0	500	8	14	1.14	2.10
centric C_8	500	8	14	1.07	1.82
centric C_{16}	500	8	14	1.06	1.45
sequential	500	8	14	1.02	0.86
sequential	0	8	9	1.00	1.00
sequential	0	8	14	1.02	0.83
sequential	0	12	9	1.00	1.30
sequential	0	12	14	1.00	1.13

Table 7.1: Signal enhancement for fat and muscle. The signals have been normalized against the $TR=8$ ms scan with sequential order and $\alpha=9^\circ$.

It is important to note that the different experiments enhance stationary tissue according to the pattern of k -space chosen. Even if the overall signal for a specific experiment increases, the parameter that should be taken into account is the change in contrast-to-noise between flowing material and surrounding tissues. If the latter remains unchanged for the conventional TOF experiment and the syncopated acquisition, the distortions caused to the reconstructed images due to the filtering effect produced by the changing magnetization during data collection does not justify the usage of short repeat times and the addition of TW but using a longer TR with the same data acquisition time as the former to enhance the flowing signal. Nevertheless, the reordered k -space data definitively enhances the signal for blood as can be seen in the comparisons of Figure 7.17 and the signal from muscle, such as demonstrated in Table 7.1.

7.6.3 Flow Enhancement with a Short TR Time-of-Flight Sequence

For completeness with the scenario presented so far, a comparison between two different TR 's and flip angles is presented. Figure 7.19 depicts the influence of TR and flip angle for a standard TOF sequence setup (for which $TW=0$ ms has been set for the syncopated excitation, and TR modified accordingly). The profile along the left carotid artery is demonstrated in the plot of Figure 7.20 for the cases shown in Figure 7.19, respectively.

The enhancement observed among volunteers varied and this effect can be alluded to the difference in heart rates and flow velocities in the carotid arteries.

7.7 Discussion

In practice, flow profiles are parabolic and the enhancement will maintain a similar shape. The repeat time and the flow rates will determine the length of the tail when the spins comply with the second condition outlined in section 7.2.

Figure 7.19: Signal along the left carotid artery as a function of TR and flip angle for a TOF FLASH sequence. (a) $TR=8$ ms / $\alpha=9^\circ$, (b) $TR=8$ ms / $\alpha=14^\circ$, (c) $TR=12$ ms / $\alpha=9^\circ$, (d) $TR=12$ ms / $\alpha=14^\circ$. The imaging parameters were: $TE=2.8$ ms, $N_y=128$, $N_x N_z=64 \times 256$, $R_x=1.05$ mm, $R_y=1.5$ mm, $R_z=3.15$ mm and $N_{acq}=3$.

Figure 7.20: Profile taken along the left carotid artery for $TR=8$ ms and $TR=12$ ms and $\alpha=9^\circ$ and $\alpha=14^\circ$. Evaluation every 1 cm.

The effects of TW with a gaussian profile are extended as better inflow can be seen as if an ideal rectangular profile was used for excitation. The signal varies more slowly with this profile during the approach to equilibrium since smaller flip angles are seen during inflow and does not saturate the signal as quickly as other profiles do.

The discontinuity seen in the simulations for higher k -space values is directly related to the presence of TW . The size of the discontinuities in the enhancement profiles is more accentuated when flowing spins see a varying flip angle along the profile, further enhanced when the excitation profiles deviate from the more ideal profile.

This situation is rather useful for pulmonary imaging since background tissue does not have any signal and the benefits of TW can be better appreciated. For other angiographic applications in the body, care must be taken since stationary tissues surrounding the vessels gain some signal back during TW and the contrast might not be that much higher than that during a continuous excitation with a TR matching the same acquisition times as the syncopated acquisition.

The choice of TW will depend on the range of flow velocities along the vessels of interest. Slow flowing blood does not benefit from inflow as much as faster spins do and remains fairly saturated even in the case of a syncopated excitation. Nevertheless, the addition of TW helps the signal from slow moving blood to be enhanced only from T_1 regrowth during TW , that in conjunction with centric k -space ordering, even without the inflow enhancement during TW , still leads to increased S/N for small vascular structures without increasing the scan time significantly. (refer to the results obtained in Chapter 6).

7.8 Summary

In this chapter, the behavior of a syncopated 3D FLASH acquisition in the case of moving spins has been investigated theoretically and the enhancement possible for flowing spins verified experimentally with the use of a flow phantom and in studies performed on volunteers.

The effects of different k -space data collection patterns were evaluated and the signal enhancement for each case quantified. Centric ordering was found to be the optimal scheme for the enhancement of blood. This scheme helps counteract, to a certain degree, the saturation effects of short TR sequences with relatively high flip angles by collecting the data during the approach to equilibrium.

Chapter 8

2D MRI Techniques in the Evaluation of the Pulmonary Vasculature: A Review

8.1 Anatomical and Physiological Studies

Early applications of MRI techniques have consisted of the evaluation of the anatomy of the pulmonary vessels using T_1 and T_2 weighted multislice SE sequences. This was also the case after velocity compensation techniques [41] made it possible to enhance signal from moving blood [52]. SE sequences demonstrate excellent anatomical views of the central and proximal pulmonary arteries and veins, providing high contrast between vessel walls and blood. This contrast allows a pulmonary embolus to be depicted as a focus of intermediate to moderately high signal mass within the vessel lumen, such as depicted in Figure 8.1, showing a central pulmonary embolus obstructing the right pulmonary tree.

While central pulmonary emboli can be identified, the SE technique may as well produce residual signal from slowly moving blood that may be confused with clot. Smaller peripheral emboli usually appear surrounded by hemorrhage and, in some cases, these emboli must be differentiated from other pathological processes with increased signal such as mucous accumulations present in the airways [15]. The latter confuses the diagnosis due to the signal and distribution similarity between vessels and

bronchi. SE images may also suffer from severe ghosting artifacts during respiration from surrounding thoracic fat, obscuring, in many instances, vessel information [53].

Figure 8.1: The SE technique provides excellent vessel wall/blood contrast that allows to visualize easily pulmonary emboli. A Central pulmonary embolus is depicted here as a region of higher intensity as compared to surrounding tissues (arrow). Note that the clot has a shorter T_1 than muscle, and consequently lower than the T_1 of blood. A multislice SE scan was utilized with an effective $TR=700$ ms and $TE=22$ ms with $N_y=192$, $R_y=2.1$ mm, $N_x=256$, $R_x=1.57$ mm, $R_z=8$ mm and $N_{acq}=3$.

Cine gradient echo imaging has been performed in an attempt to observe both morphologic and dynamic flow related information in the pulmonary vasculature [5, 6, 13]. Throughout the cardiac cycle, pulmonary emboli are typically demonstrated as regions of low intensity (Figure 8.2) that do not vary their signal when compared to surrounding flowing blood. Susceptibility related effects caused by the presence of extensive areas of air/tissue interface, turbulence and slow flowing blood may produce regions of low signal that might be confused with pulmonary emboli. Saturation effects

in vessels parallel to the imaging plane can also attenuate the blood signal such that it makes it isointense with clots, particularly at the end of the diastolic phase.

Figure 8.2: A central pulmonary embolus is demonstrated in a ROAST cine acquisition on the same patient of Figure 8.1 as a darker structure within the bright signal from blood in the right branch of the main pulmonary artery. The imaging parameters were: $TR/TE=60/12$ ms, $\alpha=60^\circ$, $N_y=128$, $R_y=3.12$ mm, $N_x=256$, $R_x=1.57$ mm, $R_z=7$ mm and $N_{acq}=3$. The phase of the image corresponds to a trigger delay of 250 ms from the R wave.

To provide a better depiction of clot and, at the same time, reduce the dependence of the image contrast in physiological parameters, the problem of pulmonary embolism detection has been attacked by applying SE sequences in conjunction with tagging techniques such as SPAMM (SPATial Modulation of Magnetization) [54], to follow the evolution of a grid pattern generated over stationary and moving tissues during the different phases of the cardiac cycle [55]. The grid pattern is maintained over stationary tissues and clots, while it disappears completely in flowing blood after the acquisition

of several phases. The spacing used for the grid in relation to the size of the clot can be problematic in the evaluation of smaller clots in distal branches.

8.2 MR Pulmonary Angiography

Time-of-flight and phase contrast techniques have been widely used to acquire MR angiograms. To date, only 2D and 3D TOF techniques have been accommodated to assess the pulmonary vasculature given that data acquisition times can be made substantially shorter than those of phase contrast methods.

The TOF MRA pulmonary techniques that are in current evaluation stage have been developed focusing on, specifically, the detection of pulmonary embolism. Special attention has been devoted into the design of techniques which minimize the image dependence on cardiac and respiratory motion as well as patient's physical condition and discomfort. Here the 2D angiographic techniques used to date are summarized.

8.2.1 2D Imaging of the Pulmonary Vasculature

A number of 2D techniques have been contemplated to assess the pulmonary vascular system. Visualization of the vessels with a positive blood/tissue contrast was first possible with the introduction of motion compensated gradient design [41, 56]. The latter was applied to pulmonary imaging using a velocity and acceleration compensated (read and slice select) 2D SE sequence [52]. An example is shown in Figure 8.3.

The technique demonstrates the pulmonary vascular tree with images that bear resemblance to those routinely acquired with X-ray computed tomography in the axial plane. Shorter echo times and thicker slices are used to avoid the washout of excited spins from the imaging slice. Poor arterial/venous as well as vessel/clot contrast does not offer a great advantage for this technique to clearly demonstrate pulmonary emboli. To improve vessel/clot contrast, the same SE technique could be used to acquire a single thick slice for which the signal from blood is decreased by using saturation pulses outside the imaging volume (similar to one of the approaches taken for 3D in Chapter 10).

Motion compensation helped in reducing ghosting artifacts from surrounding thoracic fat and improve vessel definition but vascular information was compromised in many cases due to the presence of excessive blurring and remnant ghosting.

Figure 8.3: Velocity and acceleration compensated SE sequence in both slice select and frequency encoding. Motion compensation minimizes dephasing from moving blood and presents an image with a positive vessel contrast. Motion compensation also helps reduce ghosting artifacts from surrounding thoracic fat and improve vessel resolution. The imaging parameters are: $TR=850$ ms (averaged TR computed over the whole data acquisition time), $TE=22$ ms, $R_z=20$ mm, $N_y N_x=192 \times 256$, $R_x=1$ mm, $R_y=1.5$ mm. $N_{acq}=4$.

Evaluation followed using velocity compensated GE sequences in order to enhance inflow effects, reduce imaging time with shorter TR and avoid ghosting artifacts by acquiring the data during breatholding. A considerable enhancement of the pulmonary vasculature was possible during the breathold period owing to the sufficient inflow of non-saturated blood to the imaging slice.

Initial trials used a ROAST sequence with relatively long TRs (in the order of 25-35

msec), long TE (15 ms) and intermediate flip angles ($20\text{--}40^\circ$) collecting a single slice (5–10 mm) per breatholding period [53]. This technique required several breatholding trials to cover the entire extent of the lung. Multiple breatholding periods lead, inevitably, to vessel misregistration due to the subject's inability to breathold in the same location. At the same time, imaging using surface coils was introduced to increase the signal for distal branches.

The latest introduction of more powerful gradient systems with faster switching times and new software modifications made it possible for ultra-short TR GE sequences to acquire data faster and hence image the lungs in a single breatholding period.

One approach considers the use of sequential data acquisition (see Figure 8.4) with ultrashort TR FLASH sequences and cardiac triggering [57, 58]. The use of short TR is known to produce blood signal saturation during data acquisition but to allow for better S/N and maximum arterial enhancement, the central k -space lines are acquired during the peak inflow at systole. To cover the entire lung efficiently, the acquisition proceeds sagittally from the lateral edge of the lung towards the mediastinum. The venous blood can be easily suppressed by using a single saturation pulse, located parallel and downstream to the imaged slice (Figure 8.4c). Since the acquisition is performed using cardiac triggering, total acquisition time depends on the heart rate and its variability.

To overcome saturation effects, another approach makes use of long TR and short TE sequences in a multislice format capable of collecting, effectively, the same number of slices as in the technique described above [14]. This technique does not support cardiac triggering. Consequently, ghosting from pulsating blood, further enhanced with the use of higher flip angles, is present in the resulting images. This technique has been used in conjunction with contrast agents to benefit from the T_1 shortening of blood during the first seconds after contrast injection to enhance the vessel information. Cardiac triggering could be employed in order to reduce pulsation artifacts and permit synchronized data acquisitions, producing also maximum enhancement in the pulmonary arteries. Acquisition would proceed by encoding the first slice at the edge of the lung

and continuing toward the mediastinum.

Figure 8.4: Sequential data acquisition with ultrashort TR sequences and cardiac triggering. To allow for maximum arterial enhancement, the central k -space lines are acquired during the peak inflow at the end of systole. To cover the entire lung efficiently, the acquisition proceeds sagittally from the lateral edge of the lung towards the mediastinum (b). The venous blood can be easily suppressed by using a single saturation pulse, located parallel and downstream to the imaged slice (c).

Nevertheless, the use of cardiac triggering augments the imaging time since only a single phase encoding is usually acquired per cardiac period, making it difficult to perform breathhold studies. It is possible to acquire multiple phase encodings per slice, N_p , within the same cardiac cycle to shorten the imaging time such as demonstrated in the diagram of Figure 8.5.

Figure 8.5: Multislice technique using longer TR and short TE . A breathhold study can be done by selecting TR 's on the order of 100-150 ms and encoding from 10-15 slices. Cardiac triggering is not used to keep the acquisition time short. Unfortunately, the use of high flip angles to maximize the signal from vessels may introduce pulsation artifacts. Since conventional cardiac triggered scans take longer to acquire with this setup, ghosting and cardiac motion can be avoided by using cardiac triggering and multiple phase encodings per slice within the same cardiac period. This would allow the technique to have acquisition times similar to those using the sequential 2D approach and allow for optimal signal enhancement. N_p indicates the number of phase encoding lines acquired per slice within each cardiac interval. Acquisition would proceed by encoding the first slice at the edge of the lung and continue towards the mediastinum.

Chapter 9

Relaxation Properties of Blood and Blood Clots

Blood is the part of the circulatory system that is in charge of the distribution of oxygen and substances absorbed by the digestive track, as well as the collection of CO_2 and other metabolic byproducts to the lungs and kidneys, respectively.

This chapter reviews the properties of blood and the processes that determine its relaxation characteristics and appearance in its different oxidation stages.

9.1 The Composition of Blood and Effective Proton Density

Blood is a cellular suspension. It consists of a pale yellow liquid, the plasma, in which the microscopically visible elements: the erythrocytes, or red blood cells (RBC), the leukocytes, or white blood cells; and the trombocytes, or blood platelets, are contained.

The RBCs constitute the major proportion of the cells in blood, an approximate 99% of the total count. The viscosity of blood depends in major proportion to the hematocrit H , the characteristic percentage of red blood cells to blood volume. The hematocrit averages to 47 in healthy man and 42 in woman, respectively. The normal viscosity of blood is approximately 3 times that of water although it depends mainly on its flow velocity, tremendously increasing as the flow velocity decreases (with an apparent viscosity as much as ten-fold at the level of the capillaries). The RBCs contain

about 70% water and 30% hemoglobin, excluding trace constituents.

The plasma consists of approximately 93% water and 7% protein, mainly in the form of albumin and globulin. It represents approximately 55% of the blood volume and its viscosity is about 1.5 times that of water.

The NMR signal of blood is proportional to its water density. The water content of blood is not that much different from that of other tissues and constitutes, approximately, a 78% of its total volume.

9.2 Relaxation Properties of Blood

The relaxation rates in blood, $1/T_1$ and $1/T_2$, have been found to be a linear function of the hematocrit H . This is a direct consequence of the fast exchange occurring between the intracellular and extracellular water due to the random passage of water molecules, particularly, between the plasma and the RBCs [59, 60, 61].

The relaxation rates of blood, R_{blood} , depend predominantly on the relaxation rates of the RBCs ($1/\tau_c$) and plasma ($1/\tau_p$), weighted by the relative population of protons existing in each environment, f_c and f_p , respectively. Thus,

$$\begin{aligned}
 R_{blood} &= \frac{f_c}{\tau_c} + \frac{f_p}{\tau_p} \\
 &= \frac{H}{\tau_c} + \frac{1-H}{\tau_p} \\
 &= \frac{1}{\tau_c} + H\left(\frac{1}{\tau_c} - \frac{1}{\tau_p}\right)
 \end{aligned} \tag{9.1}$$

The relationship between hematocrit and the blood relaxation rates is plotted in Figure 9.1 (taken from Reference [59]). Table 9.1 demonstrates the relaxation rates for blood and plasma (taken from Reference [59]). The values quoted in table 9.1 indicate that the T_1 relaxation of blood is approximately 1100 ms and T_2 around 200 ms, in close agreement with the values used in the simulations.

Figure 9.1: Relaxation rates ($1/T_1$) and ($1/T_2$) of blood as a function of hematocrit at 23°C.

Variable	($1/T_1$) (s ⁻¹)	($1/T_2$) (s ⁻¹)
Anticoagulant		
Plasma		
EDTA	0.57	2.2
Citrate	0.56	1.9
Heparin	0.64	2.2
Blood		
EDTA	0.89	5.5
Citrate	0.96	4.5
Heparin	0.94	5.5

Table 9.1: Relaxation rates for blood and plasma. T_2 measurements performed with a Carr-Purcell-Meiboom-Gill sequence using an interpulse spacing of 3 ms. EDTA = sodium ethylenediaminetetraacetate, citrate = sodium citrate.

9.2.1 Paramagnetic Relaxation Effects

Paramagnetic relaxation effects are usually not seen in tissues in most MRI studies. Not even the paramagnetism of dissolved O_2 found in all tissues, for example, contributes majorly to their relaxation times. Blood is an exception in that its properties are strongly coupled to the presence of hemoglobin (Hb) in the RBCs, and its oxidation states. The relaxation in whole blood is similar to that of a Hb solution, despite the effects of membrane exchanges and of plasma proteins [62].

As introduced in Section 2.4.4, the proton paramagnetic enhancement will be related to the strength of the paramagnetic dipole (the number of unpaired electrons), the electron spin relaxation rate (T_1 of the electron), the concentration of paramagnetic dipoles, the average distance from surrounding water protons, and the relative motion of proton and paramagnetic centers [63, 64]. These factors modulate the strength of the interaction between Hb in the RBCs and nearby water molecules and will be the main determinants of the relaxation properties of blood.

9.2.2 The Hemoglobin (Hb)

Hemoglobin is the red pigment of the RBCs that transports the oxygen. It is a protein with a molecular weight of 64450 and it is the predominant macromolecule in blood. Its net concentration is of approximately 15 g/100 ml (16 g/100 ml in man and 14 g/100 ml in woman) and it appears with an intracellular concentration in the order of 38 g/100 ml, or 5.5-6 mM.

The hemoglobin is constituted by four subunits, each subunit containing a heme iron conjugated with a polypeptide chain, usually referred to as the globin portion of the molecule. Each heme iron can bind, reversibly, an O_2 molecule.

9.2.3 Reactions of Hemoglobin

Hemoglobin fixes free O_2 to form oxyhemoglobin (oxyHb) when the O_2 binds to the heme iron in its reduced ferrous state (Fe^{++}). Hemoglobin alternates between

oxyhemoglobin and deoxyhemoglobin (deoxyHb) as the oxygen is exchanged between RBCs in the lungs and capillaries.

When the blood is exposed to certain drugs, or oxidizing agents in vitro or in vivo, the ferrous iron (Fe^{++}) of the molecule is converted into ferric iron (Fe^{+++}) forming methemoglobin (metHb). In the circulation, some oxidation of deoxyHb occurs transforming a portion of the deoxyHb into metHb. Nevertheless, an enzymatic system in the RBCs, the NADH-methemoglobin reductase (NADH is the reduced form of nicotinamide-adenine dinucleotide), converts the metHb into deoxyHb again. With continued oxidative denaturation, metHb is further reduced to derivatives known as hemichromes.

9.2.4 Relaxation Characteristics of Blood Products

In blood, the paramagnetic properties are confined to the RBCs. DeoxyHb and metHb are paramagnetic because they contain unpaired electrons, while oxyHb is not, given that the heme iron electron spin is canceled by the oxygen electron spin. Hemichromes do not have unpaired electrons like metHb does, so the molecule is not paramagnetic.

The paramagnetism of deoxyHb and metHb can affect the relaxation times in two ways. The first is seen in deoxyHb and metHb, and it manifests itself as a shortening in the T_2 relaxation time, consequence of the presence of increased field inhomogeneities. This is caused by the concentration of Hb in RBCs which produces microscopic magnetic field inhomogeneities that increase the dephasing effects of diffusing molecules between the RBC interior and the extracellular plasma [60, 62, 65]. Even with the use of SE sequences, the effect is marked because water molecules diffuse to regions with very different magnetic field strengths within small distances during the interpulse interval that increases phase dispersion, even more when the field inhomogeneities are not static, as in this case.

The dependence of T_2 has been investigated with a Meiboom-Gill-Carr-Purcell pulse sequence [60] and has provided an estimate for the mean residence time of water

inside the RBC of about 10 ms [60]. The T_2 shortening and susceptibility effects are better seen with gradient echo sequences [66], producing major signal attenuation with increasing echo times and, thus, a good indicator of the field inhomogeneities present. The T_2 relaxation enhancement increases as the square of the local field gradient and it has been demonstrated to be as much as 1.6 times stronger for intracellular metHb than for intracellular deoxyHb [65]. Biologic field gradients are due to heterogeneity in magnetic susceptibility and are directly proportional to the applied field. The T_2 relaxation of RBC lysates does not change with different field strengths due to the elimination of the susceptibility effects once present when RBCs were intact.

On the other hand, the direct magnetic interaction between the water protons with unpaired electron spins reduces the T_1 relaxation time, such as in the case of metHb (distances between Hb and water molecules well within $3\text{\AA}$ apart). This effect is not possible in deoxyHb because the water molecules cannot approach the heme iron closely enough to produce an important contribution to the proton relaxation enhancement. Much of the T_1 relaxation enhancement is also caused due to the electron spin relaxation time of metHb, which is closer to the Larmor frequencies used in MRI [64].

Table 9.2 summarizes the changes in the relaxation times for the different stages of oxidation of blood as compared to intact blood (taken from Reference [67]).

	T_1 (s)	T_2 (s)
Intact RBC with oxyHb	=	=
Intact RBC with deoxyHb	=	≪
Intact RBC with metHb	≪	≪
Free metHb	≪	>
Hemosiderin	=	≪

Table 9.2: Relative change in the relaxation times for blood for different stages in the oxidation process. > indicates prolongation of relaxation time; ≪ marked shortening; = no change.

9.3 Characteristics of Blood Clots

9.3.1 Mechanisms of Clot Formation

The formation of a blood clot is one of the homeostasis mechanisms that prevents the blood loss. The clot formation is immediate, within the first 20 seconds, if vascular trauma is severe, while in minor trauma the reaction is slower, between 1 and 2 minutes.

Substances present in blood and tissues have the ability to promote coagulation, called procoagulants, and others inhibiting coagulation, called anticoagulants. The balance between these two substances dictates whether blood coagulates or not. After trauma, the action of blood procoagulants is greater and initiates clot formation at the damaged site. Clot formation can also occur when a small excess in thrombin and procoagulants are present in blood, especially in slow flowing regions.

Clotting takes place in three essential steps [51]: First, a substance or complex of substances called *prothrombin activator* is formed in response to rupture of a vessel or blood itself. Second, the prothrombin activator catalyzes the conversion of prothrombin into thrombin. Third, the thrombin acts as an enzyme to convert fibrinogen into fibrin threads that enmesh platelets, blood cells, and plasma to form the clot itself.

Upon clot formation, two separate events can be started: the clot is invaded by fibroblasts, forming connective tissue all through the clot and continuing to complete organization of the clot into fibrous tissue within approximately seven to ten days, or it can dissolve when special enzymes within the clot itself are activated accordingly.

9.3.2 Appearance of Blood Clots

The proportion of fibrin, platelets, RBCs and other components varies for every clot and over time as Hb progresses from its oxygenated state to deoxyhb, to metHb, and finally to hemisiderin. Acute intracerebral hemorrhage contains blood at varying stages of clot formation and retraction and the effects on the relaxation times are depicted in Table 9.3 (taken from Reference [64]), showing the form of hemoglobin that prevails

for each clot formation stage. The relaxation rates for blood and plasma before and after clotting are summarized in Table 9.4 (from Reference [59]).

Stage	Time	Comp.	Hemoglobin	T_1	T_2
Hyperacute	≤ 24 h	Intra	OxyHb	low	high
Acute	1-3 d	Intra	DeoxyHb	isointense	low
Subacute					
Early	3+ d	Intra	MetHb	high	low
Late	7+ d	Extra	MetHb	high	mildly high
Chronic					
Center		Extra	Hemichromes	Medium	Medium
Rim	14+ d	Intra	Hemosiderin	low	low

Table 9.3: Appearance of hemorrhage at different stages of clot formation. Signals on T_1 and T_2 scans as compared against white matter. (Comp. = composition / intracellular / extracellular)

	$(1/T_1) (s^{-1})$	$(1/T_2) (s^{-1})$
Plasma		
Before clotting	0.61	2.0
Unretracted clot	0.58	2.0
Retracted clot	0.6	4.8
Blood		
Before clotting	0.80	5.5
Unretracted clot	0.83	5.8
Retracted clot	1.2	10.5

Table 9.4: Relaxation rates for blood and plasma before and after clotting. T_2 measurements performed with a Carr-Purcell-Meiboom-Gill sequence using an interpulse spacing of 3 ms.

9.4 Summary

This chapter has reviewed the characteristics of blood and clots and the factors that influence their relaxation properties. The relaxation properties of blood are mainly determined by the red blood cell count or the hematocrit, and, in essence, by the molecular interactions between the hemoglobin, one of the main constituents of the red blood cell, and the surrounding water.

Chapter 10

Evaluation of the Pulmonary Vascular System with 3D MRI: Materials, Methods and Results

This chapter describes the methodology and the results obtained on the pulmonary vascular tree of healthy individuals and patients with suspected pulmonary embolism with the syncopated 3D FLASH and 3D IR-FLASH techniques introduced in Chapter 4. The tools and facts elucidated in Chapters 6 through 7 were used to help understand the benefits and drawbacks of these techniques during the characterization of the pulmonary vasculature.

10.1 Facilities and Equipment

10.1.1 Instrumentation

Most studies were performed on a clinical 1.5 Tesla whole-body MRI unit (Magnetom SP, Siemens Medical Systems, Erlangen, Germany) operating at a resonance frequency of 63.85 Mhz and installed at the magnetic resonance facility in University Hospitals of Cleveland (Cleveland, Ohio). A limited amount of studies were conducted in a companion 1.0 Tesla system with the same hardware and software capabilities working at a resonance frequency of 42.57 Mhz.

The gradient system included current amplifiers delivering a maximum of 10 mT/m

with trapezoidal gradient waveforms and programable ramp up and ramp down times with a maximum of 1 mT/m/100 μ sec in all orientations. Pre-emphasis circuits were available to compensate gradient distortion from eddy current build up on the gradient coils.

A sequence generator program, PARGEN (PARAmeter GENerator), included with the operating system made it possible to specify the gradient waveforms and timings for the slice select, phase and frequency encoding directions for all sequences developed. Imaging parameters such as TR , TE , flip angle, matrix size, number of acquisitions, and others, such as the receiver gain and image scaling factors, were specified with a menu driven selection at the operators console.

10.1.2 Signal Reception

In most of the studies performed, images were acquired with the quadrature polarized transmit-receive body coil. To increase S/N, a set of surface coils were utilized depending on the imaging region. For the thorax, the receive only body Helmholtz coil was used on thin individuals due to size restrictions imposed by the coil geometry.

10.1.3 Study Population

The population of volunteers in the study amounted to 73 subjects with ages ranging from 18 to 50 years with a mean of 26. A population of 26 patients with ages ranging between 3 and 86 years with a mean of 53 were evaluated with pulmonary arterial disease, previously confirmed with clinical history and scintigraphic ventilation/perfusion scans (V/Q scans). One patient had a contrast angiogram study performed. Two patients were brought back for follow up studies after thrombolytic therapy. Three patients were evaluated with congenital heart disease (CHD), one with pulmonary hypertension (PAHTN) and 22 patients with suspected pulmonary embolism. Informed consent was obtained for all studies.

10.2 3D Imaging

During this work, it was found that in order to optimize the study of the pulmonary vasculature with 3D imaging, the collection of an enhanced as well as a suppressed view of the vessels represented the most convenient setup to allow for better conspicuity in vessel disease detection [68]. This is not surprising considering previous efforts involved in studies of the pulmonary vascular system with 2D imaging [55, 69]. It was found that the techniques best suited for the evaluation of vessel integrity and intraluminal masses were comprised by those techniques in which the signal from blood, rather than appearing with positive signal, had negative signal instead.

10.2.1 Early Trials

Prior to exploiting the C/N and S/N possible with data acquisition during the approach to equilibrium, MR angiograms were attempted using standard 2D and 3D GE TOF sequences based on FLASH and ROAST, with imaging parameters that have been previously optimized [70] for angiography in the head and neck. Breathholding was utilized for 2D data collection to avoid motion artifacts. In the latter, the quality of the acquisitions was hampered by the poor S/N obtained in the body coil and the presence of susceptibility artifacts, making this approach not feasible. 3D was considered a good candidate to circumvent some of these problems but it was quickly found that the standard angiographic protocols were unable to produce a clear view of the pulmonary vasculature due to the excessive motion present that destroyed the underlying vascular information. The effect of motion with standard 3D angiographic techniques is nicely demonstrated in Figure 10.10, comparing the latter with the final 3D approach implemented using very short TR , further discussed in Section 10.2.2 and in the remainder of this Chapter.

The demonstration of clots within the pulmonary vasculature in patients with suspected pulmonary emboli played a major role in determining the type of protocols for pulmonary vascular evaluation. Potential candidates from available 3D GE techniques

were realized, disregarding the nature of technique, as long as its contrast and magnetization dynamics allowed to perceive the presence of clots or pulmonary emboli. This indicated that 3D GE sequences providing either positive or negative signal for blood were openly valid to approach the evaluation of pulmonary embolism.

As described earlier, initial approaches were designed to collect bright blood images so that the MR angiogram was close in appearance to the routine contrast angiogram performed and therefore, have a similar interpretation. Initially the idea was to demonstrate signal voids in the MR angiogram corresponding to the position of the clots (as demonstrated in Figure 8.2).

The “black” blood approaches considered using standard 3D GE sequences capable of delivering suppressed blood vessels and bright clot (see Figure 8.1) are numerous. The ones used in early trials have been classified in two groups:

1. Those techniques that selectively eliminate the signal from blood flowing into the imaging slice by using presaturation bands placed close to the sites of inflow. The presaturation bands can be used advantageously to suppress the anterior thoracic chest wall and aid in the reduction of ghosting artifacts arising from moving fat. This approach has the drawback that the signal for blood may be inhomogeneous inside the imaging volume if the presaturation bands affecting the inflowing blood are not driven with the same flip angle that excites the blood inside the imaging volume.
2. Techniques known to be sensitive to motion. Those based on SSC techniques such as ROAST and CE-ROAST, or the ones that utilize motion sensitizing gradients to dephase the signal from moving spins. The more motion sensitive CE-ROAST sequence was evaluated but it was found that its motion sensitivity was difficult to control for applications in the thoracic region. The acquisitions demonstrated poor S/N and all the contents within the thoracic cage were suppressed. This was advantageously used to create a mask that helped eliminate the thoracic wall in

bright blood acquisitions automatically without having to manually segment the thoracic wall before the MIP processing (see Section 11.7).

Another approach which is virtually independent of the imaging sequence utilized (excluding CE-ROAST) is the analysis of the behavior of flowing and stationary spins from phase images since the phase of moving spins is different from that of stationary tissue. On this basis, moving blood could be easily distinguished from stationary clot. Work was performed only on several volunteers, observing, in many cases, phase changes close to regions of air-tissue interfaces (phase variation due to changes in magnetic susceptibility). The susceptibility present in clots (such as discussed in Section 9.2.4) could play an important role in helping enhance the phase differences between moving blood and stationary clot, and hence allowing for a better differentiation. This approach was not pursued aggressively.

10.2.2 3D Pulmonary Vascular Imaging with Magnetization Preparation

The final, rapid 3D GE techniques implemented to characterize the pulmonary vascular system exploit the contrast differences between tissues generated during the approach to equilibrium of the spin system upon a magnetization preparation period using the techniques explored in Chapter 4. This makes it possible for “bright” blood and “black” blood images to be generated for the study with small differences in the imaging parameters and sequence structures used. These are described as follow,

- The “bright” blood technique utilizes the proton density/inflow weighted syn-copated 3D FLASH acquisition [71]. Figure 4.5 demonstrated a block diagram characterizing this technique. The enhancement of the vasculature is produced similarly to a 3D TOF sequence differing only in that the recovery time TW is added between each in-plane phase encoding step collected to enhance inflow and counteract the saturation effects of short TR acquisitions. Several k -space trajectories are used to optimally acquire the contrast developed during the approach

to equilibrium (refer to Sections 7.2, 7.5 and 7.6). By varying TW , more or less fresh blood spins can move into the imaging slab to further enhance the vasculature while maintaining some degree of signal suppression for the stationary tissue remaining in the imaging volume.

- The “black” blood technique considers the T_1 weighted 3D IR-FLASH (Inversion Recovery FLASH). An inversion pulse (180°) is added prior to data acquisition for each in-plane phase encoding step to introduce heavy T_1 weighting. The acquisition is structured similarly as for the syncopated FLASH sequence described above. The inversion time TI is chosen to reduce or completely suppress the signal from blood such that short T_1 tissues within the blood vessels can be easily discriminated (recall Figure 8.1). This is very much the 3D extension of previous work that considered this contrast with standard SE in order to verify the presence of pulmonary embolism [3, 4, 5].

10.2.3 Data Acquisition and Image Post-processing

General Sequence Characteristics

The 3D GE sequences used for pulmonary vascular MR are characterized by using very short TR 's, varying between 5-9 ms, and short TE 's between 2-4 ms. To accomplish a short TE 's with a conventional 10 mT/m gradient system, a gaussian excitation using short RF excitation times between 256 μ sec and 1024 μ sec and an asymmetric echo with 16-45 points collected before the echo are used. To allow for the shortest TE possible, flow compensating gradient waveforms are eliminated and it is assumed that the flow dephasing is small and the intravoxel dephasing is minimal (see Section 5.4) Partial flow compensation can be used at the expense of longer echo times [70].

The readout period for this setup is shorter than in conventional imaging for the technique to accommodate the short repeat times, but long enough that in conjunction with the gradient system, small FOV imaging is possible. This corresponds to imaging with readout bandwidths between 195 Hz/pixel and 244 Hz/pixel with sampling rates

as low as $8\mu\text{sec}$ to a maximum of $20\mu\text{sec}$ for 256 points and a minimum FOV of 175 mm along the frequency encoding axis (t_{ADC} of 5.120 ms and 4.096 ms, respectively). Randomized RF spoiling is used [33] to minimize the duration of the spoiler gradients after the readout period as to further decrease TR .

Sequence Setup

The syncopated acquisition using FLASH or 3D IR-FLASH are designed to perform an axial or sagittal excitation over the thorax, followed by a coronal slice select phase encoding as shown in Figure 10.1a and Figure 10.1b, respectively. The axial excitation covers both lungs and the mediastinum in the craniocaudal direction. The frequency encoding is performed along the x -axis (laterally), the in-plane phase encoding along the z -axis (craniocaudally) and the coronal slice select encoding along the y -axis (or partition encoding direction, collected along the anteroposterior direction), respectively, as indicated in Figure 10.1a. For the sagittal excitation scheme, only one lung is imaged at a time and the slab is centered in the middle of each lung. Here, the frequency encoding is performed along the craniocaudal direction while the in-plane phase encoding is done laterally, such as shown in Figure 10.1b. The thickness of the slice excited is the effective FOV used in the in-plane phase encoding direction for both schemes.

Slice selection is accomplished by applying a $640\mu\text{sec}$ RF excitation during the application of a constant gradient pulse of 2mT/m in the in-plane phase encoding direction before applying the in-plane phase encoding table. This can be seen in the sequence diagrams of Figures 10.2a,b for the axial and sagittal excitation schemes, respectively.

Figure 10.1: Encoding directions for an axial and a sagittal excitation, coronal readout schemes. The axial excitation (a) is used to cover an approximate volume of 10-16 cm containing both lungs and the mediastinum. The frequency encoding is performed along the x -axis (left to right), the in-plane phase encoding along the z -axis (craniocaudally) and the coronal slice select encoding (2nd phase encoding) along the y -axis (anteroposteriorly), respectively. For the sagittal excitation scheme (b) a 10 cm excitation is used. The frequency encoding and in-plane phase encoding are interchanged relative to the ones used for the axial excitation scheme. The setup allows the collection of coronal slices without the problems of aliasing for small FOV.

Figure 10.2: Sequence diagrams for axial excite (a) and sagittal excite (b), coronal read sequences. Slice selection occurs during the application of an RF excitation and a constant gradient pulse of 2mT/m in the in-plane phase encoding direction before applying the in-plane phase encoding table. The in-plane phase encoding table is applied along the z and the x -axis for the axial and the sagittal excitation, respectively (the gradient waveforms between the axial and sagittal scans are swapped).

Typical Acquisition Parameters and Imaging Time

The volume excited is chosen to be 10-16 cm for the axial excitation and 10 cm for the sagittal excitation. With this setup, the whole volume must be encoded to avoid aliasing in the anteroposterior direction (the partition encoding direction). Usually, a fixed encoding thickness of 192 mm is chosen and a small degree of aliasing is allowed along this direction since only the lung cavity is of interest (aliasing would occur in the back of the spine and in the anterior thoracic wall).

Assigning L for FOV, N for number of sampled points, and R for resolution, and using the subscripts to indicate the relevant direction using the axes of Figure 10.1a, the typical parameters employed for the 3D acquisition are: $L_x=175$ -300 mm, $N_x=256$, $R_x=0.68$ -1.17mm; $L_z=100$ -160 mm, $N_z=64$, $R_z=1.56$ -2.50 mm; and $L_y=150$ -220 mm, $N_y=128$, $R_y=1.17$ -1.71 mm for an axial excitation scheme; for a sagittal excitation the roles of the x and z directions are interchanged (see Figures 10.2a,b) and a fixed $L_x=100$

mm is used. The axial and sagittal excite versions with the 3D IR-FLASH sequence are implemented in the same fashion as above but include the inversion pulse a time TI prior to the application of each complete partition loop of the FLASH sequence.

The effective 2D equivalent TR for the syncopated acquisition, TR_{eff} , is given by

$$TR_{eff} = TR_{FLASH} N_y + TW \quad (10.1)$$

For the 3D IR-FLASH scan, TR_{eff} , is given by

$$TR_{eff} = TI + TR_{FLASH} N_y + TW \quad (10.2)$$

The inversion time TI is chosen such that the blood signal is selectively minimized or completely suppressed.

Neither cardiac triggering nor respiratory gating are utilized during data collection. The reduction of motion artifacts relies on the use of pseudogating [72, 73], using multiple acquisitions with (N_{acq}) data sets collecting all the slice select phase encoding and frequency encoding data and averaged over for each in-plane phase encoding line.

The two possible positions that can be assumed by the acquisition loop in a 3D scan are demonstrated in Figure 10.3a,b. In Figure 10.3a, the acquisition loop is placed outside the partition loop so that all the slice select phase encoding steps are acquired N_{acq} times before averaging is performed on the data. Figure 10.3b demonstrates the case in which the acquisition loop is positioned inside the partition loop. For this setup, each partition is acquired N_{acq} times before stepping to the next slice select phase encoding value. Figure 10.3c shows the case for a syncopated 3D FLASH or 3D IR-FLASH scan which has a similar structure as demonstrated in Figure 10.3a but TW is added after the averaging operation is performed. The effects of the loop structure were then evaluated accordingly for all the possibilities mentioned to observe the degradation due to motion and the effects of pseudogating the data.

The acquisition loop outside the partition encoding loop and 5-8 acquisitions were previously found to be optimal and it has been the standard for all the studies performed

(see results in Section 11.3) in which k -space order and imaging parameters were varied to quantitate the effects on the signal of the pulmonary vessels. To keep imaging times reasonable, rectangular field-of-view (recFOV) (see Section 3.3.4) imaging with a reduced number of in-plane phase encoding steps is used to accommodate the high number of acquisitions needed to reduce the motion artifacts.

Figure 10.3: The two different locations that may be used for the position of the acquisition loop. (a) the acquisition loop collects all the slice select phase encoding steps N_{acq} times before performing the averaging process. (b) each slice select phase encoding value is acquired N_{acq} before the averaging is performed. (c) shows the diagram of the actual loop structure of a syncopated acquisition, a natural extension of (a) due to the introduction of TW .

Image Post-processing

Visualization of the pulmonary tree is done using a targeted Maximum Intensity Projection reconstruction (MIP). Views are reconstructed at different angles and played back in a cine loop. Multiplanar reconstructions (MPR) are used to reconstruct slices in an arbitrary orientation.

Manual segmentation of the thoracic wall is performed to show the complete vascular tree. Automatic segmentation routines can also be used but were not readily applicable to remove the thoracic region. An attempt for automatic segmentation was done by creating a binary mask using a flow sensitive syncopated CE-ROAST acquisition that

multiplied the angiographic images, demonstrated merely as a curiosity in the discussion section (Section 11.7).

10.3 Angiographic Studies in the Pulmonary Arteries of Healthy Volunteers

10.3.1 Effects of TW and Flip Angle

The effective repeat time per in-plane phase encoding step, TR_{eff} , was varied between 1050 ms and 1600 ms ($TW=0$ ms to $TW=550$ ms) for both axial excite and sagittal excite, coronal read scans for 128 partition scans to show the degree of inflow enhancement possible in the pulmonary arteries, as previously addressed in Sections 7.5.2 and 7.6 on the flow phantom and carotid arteries, respectively. The influence of TW for an axial excitation, coronal readout scheme can be visualized in Figure 10.4. Figures 10.4a,c demonstrate 2 cm thick axial MIP reconstructions from a scan using $TW=500$ ms. Figures 10.4b,d show the same region on a dataset collected with $TW=0$ ms. The introduction of TW produces an overall enhancement of blood and stationary tissue but certainly different for blood, further enhanced by inflow of non-saturated spins to the imaging volume. Both scans were acquired otherwise with the same parameters. The effects of TW for a sagittal excitation scheme are demonstrated in Figure 10.5a,b for $TW=0$ ms and $TW=350$ ms, respectively.

Signal in the arteries is enhanced according to the washin occurring during TW . The washin effect is only dependent on the average velocity of blood in the pulmonaries during the cardiac cycle, and supported by the fact that multiple acquisitions are averaged without cardiac triggering during data collection (see the effects of multiple acquisitions shown in the flow phantom results under pulsatile flow conditions in Section 7.5.2).

Veins and small vessels that do not receive fresh blood are still somewhat enhanced given that they recover partially longitudinal magnetization during TW . This extra enhancement allows them to be better visualized (compare lung apex in Figures 10.5a,b).

Figure 10.4: 2 cm thick axial MIP reconstructions from an axial excite, coronal encoding sequence comparing a scan using $TW=500$ ms ($TR_{eff}=1550$ ms) in (a) and (c) and a scan with $TW=0$ ms ($TR_{eff}=1050$ ms) in (b) and (d). During TW , longitudinal magnetization recovery and inflow occurs to enhance stationary as well as moving blood. If imaging times are made equal with all other imaging parameters the same, the $TW \neq 0$ image would show higher S/N and different vessel contrast. The longer TW of 500 ms leads to enhanced blood signal. Imaging parameters were: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.0$ mm, $R_z=1.6$ mm, $R_y=1.5$ mm and $N_{acq}=8$. The central lines of k -space were acquired using an asymmetric sequential data collection with $N_{off}=32$.

Figure 10.5: With a sagittal excitation better enhancement of the arteries is possible since less saturated blood enters the imaging slab while remaining blood in veins is saturated. (a) and (b) demonstrate the differences between a scan with $TW=0$ ms and $TW=350$ ms in a sagittal excitation. Better S/N is possible with non-zero TW and inflow effects can be noted up to the first branching of the right pulmonary artery. Even though the blood cannot be fully replaced during the short TW used, overall signal recovery in all tissues permit the visualization of smaller vessels in the lung apex (b). Centric ordering was used with 15 RF preparation cycles (C_{16}). Imaging parameters: Syncopated FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_z=1.0$ mm, $R_x=1.6$ mm, $R_y=1.5$ mm and $N_{acq}=7$.

The degree of enhancement obtained with the introduction of TW and data collection during the approach to equilibrium produces a better enhancement in the small vessels as compared to the standard 3D time-of-flight (TOF) experiment with the same acquisition parameters but having $TR=TR_{eff}/N_y$ to equalize the imaging time.

Figure 10.6: Flip angle comparison for an axial excite, coronal read sequence for a fixed $TW=500$ ms and for: (a) 7° , (b) 10° , (c) 13° and (d) 15° , respectively. The thickness of the volume excited was 12 cms and the slices were reconstructed towards the middle of the volume. Higher degree of arterial blood saturation occurs at higher flip angles since the whole heart is excited. Venous signal at the edges of the volume is further enhanced at higher flip angles. Imaging parameters were: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.0$ mm, $R_z=1.6$ mm, $R_y=1.5$ mm and $N_{acq}=8$. The central lines of k -space were acquired using an asymmetric sequential data collection with $N_{off}=32$.

The effects of flip angle on vessel enhancement were evaluated for a fixed $TW=500$ ms, and varying the flip angles from 7° to 20° . Figures 10.6a-d demonstrate the

difference in contrast behavior for $\alpha=7^\circ$, $\alpha=10^\circ$, $\alpha=13^\circ$ and $\alpha=15^\circ$, respectively. At lower flip angles, less saturation for blood spins occur and the vessels are enhanced up to the periphery of the lung. For an axial excite setup the input of unsaturated spins occur only through the superior and inferior vena cava. The distance for these spins to travel from the edge of the excited slab to the periphery of the lung is substantial since the spins have to go pass the heart to reach the main right and left pulmonary arteries and all their branching vessels. From here it is easily seen that considerable spin saturation can occur for small variations in the flip angle. This is also shown as the arterial and venous signals have similar amplitudes, making especially hard the task of separating them during an MIP reprojection. This is less of a problem in the sagittal excitation scheme, in which the blood at the level of main right and left pulmonary arteries starts its way into the excitation region.

10.3.2 The Effects of K-space Order in the Arterial and Venous Enhancement

Centric and sequential ordering were implemented to assess the contrast and signal enhancement in each case. To alleviate eddy current effects and minimize signal inhomogeneities in the images along the slice select phase encoding direction (antero-posteriorly), gradient preparatory cycles should have been incorporated before data acquisition, such as discussed in Section 6.2.1. Results on the vessel resolution phantom of Figures 6.17 and 6.18 presented the potential problems when lacking from these gradient preparatory cycles.

Gradient prepulses alone could not be realized and instead, n RF/gradient preparatory cycles, usually 7 or 15, were applied with the gradients and the RF excitation applied together before acquiring the data with centric ordering. The degree of enhancement under these conditions was, therefore, evaluated to associate the signal gain with respect to the reduction in eddy current blurring effects. The values of k -space discarded were the higher positive and negative k -space lines. For this setup, the indexes C_x are utilized to relate the acquisition to the number of RF/gradient cycles performed as previously

noted, with x indicating the RF at which the center k -space line is collected. For signal comparison, centric ordering (C_0) without any preparatory cycles was also used. Prior to the availability of centric ordering, sequential ordering was employed with the central k -space line collected after stepping through 1/4 of k -space by using an off-centered table (asymmetric sequential with $N_{off}=32$). Prior results for the asymmetric sequential case showed that vessel enhancement ranged between 1.08 and 1.25, depending on the region evaluated along the vessel path for the sagittal excite data sets collected from 5 subjects. The asymmetric sequential approach requires higher gradient strengths and introduces Gibb's ringing during reconstruction along the slice select direction (such as pointed out in Figure 10.10b).

Figure 10.7 demonstrates the different degrees of vessel enhancement possible in the right pulmonary vasculature of a healthy individual. For centric data collection, the signal enhancement for C_0 , C_8 and C_{16} are depicted in Figure 10.7a-c. The enhancement possible is clearly seen if the previous examples are compared to Figure 10.7d, collected with the same imaging parameters but with a sequential acquisition of the slice select phase encoding steps ($N_{off}=64$). Note that the benefits from data collection during the approach to equilibrium have been almost lost in Figure 10.7d, comparing it with the same acquisition but setting $TW=0$ ms such as it is shown in Figure 10.7e. These effects were previously seen in Section 7.6 with the same imaging protocol was used to verify the enhancement in the region of the carotid arteries.

Table 10.1 summarizes the signal intensities measured along the main and descending branch of the right pulmonary artery and the venous return to the heart in the regions that have been indicated in Figure 10.7a and conveniently plotted in Figure 10.8. The measurement was performed on the original, coronally acquired slices.

Table 10.2 presents the degree of enhancement possible for stationary tissues, such as fat and muscle. The signal was taken on the anterior thoracic wall from sagittal MPR reconstructions along the same data set.

Figure 10.7: Enhancement of the pulmonary vasculature with centric and sequential acquisition order of k -space. (a) C_0 , (b) C_8 , (c) C_{16} , (d) sequential with $TW=500$ ms, (e) sequential with $TW=0$ ms. Imaging parameters: Syncopated FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_z=0.85$ mm, $R_x=1.7$ mm, $R_y=1.5$ mm and $N_{acq}=6$.

The reconstructions of Figure 10.7 do not allow to visualize the smearing occurring along the slice select phase encoding from eddy current effects during data acquisition. These effects are clearly demonstrated in Figure 10.9 by taking a 2 cm sagittal MIP reconstruction along the data set from which Figures 10.7a-e were reconstructed (see to Section 6.7). Smearing is worst for the C_0 acquisition (Figure 10.9a). The smearing becomes less obvious and reduced as the number of RF/gradient preparation cycles is incremented, such as depicted in Figures 10.9b,c for C_8 and C_{16} data collection, respectively. As noted earlier, the vessel enhancement is gradually lost and tending, in the limit, to show the saturation of the vasculature with the short TR 's used but lesser effects of eddy current instabilities (Figure 10.9d).

Figure 10.8: Comparative plot from the data listed in Table 10.1 showing the enhancement in the different regions R_0 to R_6 of the pulmonary tree as outlined in Figure 10.7.

k -space order	TW (ms)	R_0	R_1	R_2	R_3	R_4	R_5	R_6
centric C_0	500	1.00	1.59	2.68	2.42	2.16	1.61	1.38
centric C_8	500	1.01	1.65	2.58	2.03	2.01	1.34	1.15
centric C_{16}	500	1.01	1.63	2.24	1.90	1.80	1.28	1.05
sequential	500	1.00	1.61	2.02	1.55	1.51	0.93	0.79
sequential	0	1.00	1.66	1.93	1.29	1.28	0.81	0.58

Table 10.1: Signals intensities in selected regions of the pulmonary vasculature using different k -space trajectories. The signals have been normalized against the $TR=8$ ms scan with sequential order and $TW=0$ ms at R_0 , where all scans present nearly the same signal due to the low flip angle from the imperfect slice profile. The evaluation regions R_0 to R_6 are indicated in Figure 10.7. R_0 - R_5 measure the signal along the path of the descending pulmonary artery. R_6 measures the signal at the vein return from the base of the lung to the heart. Some minor signal variations are attributed to the erroneous placement of the ROI due to vessel motion between scans.

k -space order	TW (ms)	Fat	Muscle
centric C_0	500	1.03	2.09
centric C_8	500	1.03	1.81
centric C_{16}	500	0.98	1.65
sequential	500	1.02	1.12
sequential	0	1.00	1.00

Table 10.2: Signals for fat and muscle in a syncopated 3D FLASH acquisition with centric and sequential k -space trajectories using the sagittal excitation, coronal readout sequence. The signals have been normalized against the signals of fat and muscle collected with sequential order and $TW=0$ ms, respectively. All scans acquired with $TR=8$ ms and $\alpha=14^\circ$.

Figure 10.9: Sagittal 2 cm thick MIP reconstructions from the sagittal excite, coronal read data set of Figure 10.7 showing the smearing effects of unstable eddy current conditions affecting the images acquired with centric data acquisition order (bright fuzziness in the background signal). Smearing is worst in (a), corresponding to the C_0 case. As the number of RF/gradient preparation cycles is incremented, the smearing becomes less, such as depicted in (b) and (c) for C_8 and C_{16} data collection, respectively. Nevertheless, vessel enhancement is diminished accordingly for increasing number of RF/gradient preparation cycles. (d) shows the sequential case. Imaging parameters: Syncopated FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=500$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_z=0.85$ mm, $R_x=1.7$ mm, $R_y=1.5$ mm and $N_{acq}=6$.

10.4 Effects of Thoracic Motion on the Resolution of Pulmonary MR Angiograms

10.4.1 Short TR and Averaging Multiple Acquisitions

The influence of the number of acquisitions and the position of the acquisition loop in 3D acquisitions was investigated to visualize the effects in pseudogating the data. The acquisition loop was placed inside and outside the slice select phase encoding steps loop for standard 3D non-synopated 3D FLASH acquisitions. Short and long TR sequences were also evaluated.

Long TR sequences are not considered to be optimal to image the pulmonary arteries ($TR \sim 25 - 50$ ms). Figure 10.10a shows the image degradation that occurs for a standard head flow imaging sequence using a $TR=30$ ms, $\alpha=15^\circ$, 64 partitions and 3 acquisitions, collected sagittally. Severe motion artifacts from the thoracic wall cross the image, further enhanced by the use of the surface coil in front of the chest. Figure 10.10b demonstrates the artifact reduction using the sagittal excitation coronal encoding scheme, collected in the same imaging time. The striping occurring along the posterior-anterior direction for Figure 10.10b is Gibb's ringing due to the asymmetry in the encoding of the slice select direction.

The effectiveness of averaging multiple acquisitions to reduce ghosting artifacts introduced by blood pulsatility and respiratory motion is demonstrated in Figure 10.11a-d, in which N_{acq} has been set to 1, 2, 4 and 6, accordingly. In this example, the predominant source of artifacts arise from blood pulsation, manifesting more intensely along the in-plane phase encoding direction (laterally) but not along the slice select (anteroposteriorly), not possible to appreciate in Figure 10.11 but confirmed with an MPR reconstruction in the sagittal plane. Flow artifacts are enhanced with higher flip angles and in part augmented due to the lack of velocity compensation gradients. As the number of acquisitions is increased, flow artifacts are continuously and better suppressed, averaging the phase errors and providing a more uniform signal and k -space

coverage. This also increases the S/N although it can be noted that the arteries and veins close to the base of the lung in the case of $N_{acq} = 6$ are blurred as compared to the case of $N_{acq} = 4$ (arrows), clearly indicating the effects of diaphragmatic motion on vessel resolution. The degree of blurring diminishes towards the apex and the vessel calibers for the scans compared are similar.

To verify correctly the influence of the number of acquisitions performed on the S/N improvement and motion artifact reduction, averaging should have been done after collecting N_{acq} single acquisition data sets so that the imaging time for Figure 10.11 could be kept shorter and maintain more stable conditions for the individual evaluated during the imaging time as opposed to having collected the data sets with the right number of acquisitions.

The craniocaudal direction remains to be the axis of major motion in normal individuals during quiet breathing and hence, the direction in which vessels blur the most. Having selected a larger FOV, the motion of the diaphragm would have been imprinted along the in-plane phase encoding, specially enhanced due to the abrupt signal change of the body Helmholtz coil at the edges of the FOV (signal reception is similar to that of a surface coil).

10.4.2 The Acquisition Loop Order

Figure 10.12a,b are compared for the same TR and number of acquisitions averaged but the acquisition loop is inside and outside of the partition encoding loop, respectively. The same short TR is used to compare with the TR used in the syncopated excitation (Figure 10.12c). In Figure 10.12b, the effective TR is not increased when collecting all the partitions as opposed to the case in Figure 10.12a. Figure 10.12b is effectively more suitable for pseudogating. Note that the introduction of TW in the syncopated acquisition enhances several vessels in Figure 10.12c as compared to Figure 10.12b.

The syncopated sequence had to be designed so that the acquisition loop occurs over the collection of the in-plane phase encoding lines. This is a natural consequence

of having a preparation period and TW included, making it possible to pseudogate the data if necessary.

Figure 10.10: Image degradation occurring with a standard FLASH angiographic sequence using long TR (a). Severe motion artifacts from the thoracic wall cross the image, further enhanced by the use of the surface coil in front of the chest. A syncopated 3D FLASH acquisition was used for (b), showing a considerable improvement in vessel definition over the scan performed in (a). Imaging times for both examples were the same. The images correspond to 2 cm thick MIP reconstructions from a sagittal excite, sagittal read and sagittal excite, coronal read schemes, respectively. The striping occurring along the posterior-anterior direction in (b) is due to Gibb's ringing, enhanced as a result of the asymmetry in the encoding of the slice select direction (asymmetric sequential data collection with $N_{off}=32$). The increased number of acquisitions helps reduce motion artifacts. Imaging parameters: for (a) FLASH 3D, $TR=30$ ms, $TE=6.0$ ms, $\alpha=15^\circ$, $N_x=64$, $N_yN_z=128 \times 256$, $R_x=1.5$ mm, $R_y=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=3$; for (b) Syncopated FLASH 3D, $TR_{eff}=1450$ ms, $TR=8.2$ ms, $TE=2.5$ ms, $\alpha=14^\circ$, $N_{prep}=7$ (C_8), $N_y=128$, $N_xN_z=64 \times 256$, $R_x=1.56$ mm, $R_y=1.5$ mm, $R_z=0.78$ mm and $N_{acq}=5$.

Figure 10.11: Effects of averaging multiple acquisitions to reduce respiratory and flow related ghosting artifacts with a syncopated FLASH acquisition. (a) $N_{acq}=1$, (b) $N_{acq}=2$, (c) $N_{acq}=4$ and (d) $N_{acq}=6$. Ghosting artifacts from respiration are difficult to visualize along both phase encoding directions since the respiratory excursion in the lateral and posterior-anterior directions is the least in normal individuals. Blurring is maximum along the frequency encoding direction (craniocaudally) but no ghosts are associated to it. Imaging parameters: Syncopated FLASH 3D, $TR_{eff}=1450$ ms, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=12^\circ$, $N_{prep}=7$ (C_8), $N_y=128$, $N_x N_z=64 \times 256$, $R_y=2.5$ mm, $R_x=3.4$ mm, $R_z=0.86$.

The same set of comparisons is done in Figure 10.13 but in this example imaging was performed in the left pulmonary tree as opposed to the previous example of Figure 10.12,

which examined the right pulmonary tree instead. Heart motion subjects the left pulmonary tree to more motion than that on the right but as depicted in Figure 10.13c, the quality of the syncopated FLASH acquisition is good enough to provide a good visualization of the main branches of the left pulmonary tree. Figures 10.13a,b show the same comparisons as in Figures 10.12a,b in which the acquisition loop is placed inside and outside the partition encoding loop, respectively. Figure 10.10b is also an example in which the acquisition loop was placed outside the slice select phase encoding loop.

Blurring is an important consideration when dealing with any scan that it is not synchronized with the physiologic signals in cases of motion. To evaluate the blurring occurring with the 3D acquisition, a comparison with respiratory gated and/or cardiac triggered data sets was done using single thick slice velocity compensated SE imaging.

(a)

(b)

(c)

Figure 10.12: Influence of the order in which the averaging loop is done in a continuous, short TR acquisition, on the right pulmonary vasculature. For (a) the averaging loop is placed inside the partition encoding loop as opposed to (b), where the averaging loop remains outside but inside the in-plane phase encoding loop. The examples are compared for the same TR and number of averages. Better image quality is consistently shown for the averaging loop outside the partition encoding loop, which corresponds to the same strategy used in the syncopated case, as shown in (c). Imaging parameters: for (a) and (b) Sagittal excite, sagittal read FLASH 3D, $TR=8.0$ ms, $TE=2.5$ ms, $\alpha=14^\circ$, $N_x=64$, $N_y N_z=128 \times 256$, $R_x=1.5$ mm, $R_y=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=8$. For (c): Sagittal excite, coronal read syncopated 3D FLASH with $TR=8.0$ ms, $TW=500$ ms, $TE=2.5$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_y=1.5$ mm, $R_x=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=7$ with C_8 . For all the examples, a 2 cm thick MIP was reconstructed sagittally.

The examples shown in Figures 10.14a-c and Figures 10.15a-c provide a comparison between a single slice SE image collected with both respiratory gating and cardiac triggering, only cardiac triggering and the MIP reconstructed in the same location

from the syncopated 3D FLASH acquisition. Figure 10.14a demonstrates a respiratory gated/cardiac triggered SE showing superb resolution in the distal branches of the pulmonary arteries (arrow). Elimination of respiratory gating produces overall blurring of the vessels in the same region (Figure 10.14b). Figure 10.14c shows the same region reconstructed from the 3D scan.

For the 3D case, the small vessels appear to have a larger diameter but the information is retained. The lower resolution of the 3D data set along the anteroposterior direction as compared to the SE also contributes to give a slightly larger vessel diameter. Figure 10.15 shows the same comparisons depicted in Figure 10.14. In this case, the reconstruction from the 3D data set (Figure 10.15c) resolves the small vessels better than both SE scans (Figure 10.15a,b). The SE scans without any physiologic synchronization provide the worst vessel detail in this set of comparisons.

(a)

(b)

(c)

Figure 10.13: Influence of the order in which the averaging loop is done in a continuous, short TR acquisition, on the left pulmonary tree. For (a) demonstrates the case in which the averaging loop is placed inside the partition encoding loop. In (b), the averaging loop remains outside. (c) demonstrates the results obtained with the syncopated excitation. Imaging parameters: for (a) and (b) Sagittal excite, sagittal read FLASH 3D, $TR=20$ ms, $TE=2.5$ ms, $\alpha=15^\circ$, $N_x=64$, $N_y N_z=128 \times 256$, $R_x=1.56$ mm, $R_y=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=4$. For (c): Sagittal excite, coronal read syncopated 3D FLASH with $TR=8.2$ ms, $TW=450$ ms, $TE=2.8$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_y=1.5$ mm, $R_x=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=7$ with C_8 . For all the examples, a 2 cm thick MIP was reconstructed sagittally.

Figure 10.14: (a) demonstrates a respiratory gated/cardiac triggered SE showing superb resolution in the distal branches of the pulmonary arteries (arrow). Elimination of respiratory gating produces overall blurring of the vessels in the same region (b). (c) depicts an MIP reconstruction from a syncopated, sagittally excited sagittally encoded data set in the same region as in (a) and (b). Imaging parameters: for (a) and (b) single slice SE, $TE=22.0$ ms, $N_y N_z=192 \times 256$, $R_x=20.0$ mm, $R_y=1.0$ mm, $R_z=0.78$ mm and $N_{acq}=3$ (acquisition time for (a) 45 min, (b) 10 min); for (c) Syncopated FLASH 3D, $TR_{eff}=1000$ ms, $TR=8.0$ ms, $TE=2.5$ ms, $\alpha=14^\circ$, $N_{prep}=7$, $N_x=64$, $N_y N_z=128 \times 256$, $R_x=1.5$ mm, $R_y=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=6$. The SE scan had in this case a higher in-plane resolution along the in-plane phase encoding direction.

Figure 10.15: A second comparison of the effects of gating. A thick slice SE using respiratory gating and cardiac triggering (a) and cardiac triggering only (b) are compared to the same slice reconstructed from the 3D data set (c). In this example, the syncopated scan gives the best results. Imaging parameters: for (a) and b) single slice SE $TE=22.0$ ms, $N_y N_z=128 \times 256$, $R_x=20.0$ mm, $R_y=2.0$ mm, $R_z=1.0$ mm and $N_{acq}=2$; for (c) Syncopated FLASH 3D, $TR_{eff}=1000$ ms, $TR=8.0$ ms, $TE=2.5$ ms, $\alpha=14^\circ$, $N_{prep}=7$, $N_x=64$, $N_y N_z=128 \times 256$, $R_x=1.5$ mm, $R_y=1.56$ mm, $R_z=0.78$ mm and $N_{acq}=6$.

10.5 Example Pulmonary MR Angiograms

The MIP reconstructions shown in Figure 10.16 demonstrate the potentials of 3D data collection even in the case of motion. The examples shown here are considered to be the best data sets acquired so far. Good vessel visualization is possible in all the regions of the lung but some blurring occurs naturally at the base due to the unavoidable motion of the diaphragm and the long acquisition times required to collect these data sets (roughly 11 minutes). The sagittal excite, coronal readout scheme was used in order to obtain the maximum enhancement for the arteries, clearly distinguished from the veins in both data sets.

Velocity compensated SE sequences have been acquired to compare the quality and resolution of the pulmonary vessels that can be obtained with a 3D scan. Figure 8.3 showed a 2 cm thick, transverse excitation, triggered, single slice SE acquisition in the region of the branching of the main pulmonary arteries on a healthy volunteer. An equivalent reconstruction covering the same region with a 2 cm thick MIP (12 slices) from the axially excite, coronally encoded 3D data set is demonstrated in Figure 10.17. Although the SE scan can potentially provide a much finer resolution for the vessels in the periphery of the lungs, even for images acquired in the body coil, the quality of the 3D acquisition is comparable and allows MPR or MIP reconstructions in any desired orientation.

Resolution can be further improved using half Fourier reconstruction methods along the frequency encoding direction in order to eliminate the Gibb's ringing and recover the loss in resolution introduced from the asymmetric echoes used during data collection. A Cuppen half Fourier algorithm [74] was applied to the first data set shown in Figure 10.16 and compared to the usual Fourier reconstruction, such as demonstrated in Figure 10.18. A clear improvement in vessel definition was appreciated along the frequency encoding (craniocaudally) of the half Fourier data set in each individual slice before the MIP reconstruction of Figure 10.18b was performed.

Figure 10.16: The right pulmonary vasculature of two healthy volunteers is demonstrated in 3 different MIP views originating from a sagittal excitation scheme. (a) and (c) show a lateral view and a frontal view of the pulmonary vasculature, while (b) is reconstructed at 66° , sagittal towards coronal. Manual segmentation of the thoracic wall and heart was performed before the MIP reconstruction. Despite the diaphragmatic motion, vessel information is retained at the lung base. The arrows indicate the more suppressed veins. Imaging parameters: Syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms $TR_{eff}=1450$ ms, $\alpha=14^\circ$, $N_y=128$, $N_x N_z=64 \times 256$, $R_x=1.56$ mm, $R_y=1.5$ mm, $R_z=0.78$ mm, $N_{acq}=7$ and C_{16} . Data collected with the Helmholtz body coil.

Figure 10.17: 2 cm thick transverse MIP reconstruction from a transverse excite, coronal read data set acquired on a healthy volunteer. Imaging parameters: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.7$ ms, $TW=500$ ms, $\alpha=9^\circ$, $N_z N_x=64 \times 256$, $R_x=1$ mm, $R_z=1.6$ mm, $R_y=1.5$ mm, $N_y=128$ and $N_{acq}=8$. Note that 13 slices were MIPed to produce the region of interest.

The improvement in resolution is usually accompanied with the expected decrease in S/N, clearly demonstrated between the images shown. This decrease in S/N does not help the MIP projection of the half Fourier data set to really show the resolution improvement, in addition to having some artificial brightening in some of the small vessels that might be misinterpreted as pulmonary emboli.

10.6 Suppressing Blood in the Pulmonary Vasculature

The syncopated 3D FLASH sequence was found difficult to interpret during the first clinical trials on patients with suspected pulmonary embolism. One reason for this difficulty is associated to the limited arterial enhancement possible in relation to the flow velocities encountered in patients having occluded vessels due to the presence of

a clot, providing little contrast between clot and surrounding blood, and those suffering from hypertension. Secondly, the shorter T_1 of clot competes with the signal from saturated blood. At last, interference from respiratory motion makes the signal from blood and clot blend, diminishing even more the possibility to differentiate the sudden differences among both.

Figure 10.18: Comparison between a normal Fourier reconstruction (a) and the same data set reconstructed with a half Fourier routine (b) to improve the resolution along the frequency encoding direction, collected usually with an asymmetric echo in order to achieve very short echo times. The acquisition parameters are the same as the previous set of images. The echo was centered 40 points into the ADC interval (256 points collected). S/N is decreased in (b) as a result of the resolution enhancement with half Fourier. The individual slices showed the improved resolution along the frequency encoding, hardly noticed in the MIP reconstruction.

Here the 3D IR-FLASH technique is utilized to minimize or completely eliminate the signal from blood. Figures 10.19a,c show two 2 cm thick axial MIP reconstructions from a syncopated 3D FLASH sequence collected with an axial excite coronal read encoding using $TW=500$ ms, and compared with the 3D IR-FLASH acquisition with $TI=300$ ms and $TW=200$ ms at the same locations (see Figures 10.19b,d). It can be appreciated that the blood signal can be substantially suppressed while shorter T_1 tissues, such as fat, maintain their signal and appear enhanced. Excluding the presence of the inversion pulse used for blood signal suppression, the imaging parameters and sequence structure are similar to those used in the syncopated 3D FLASH acquisition.

The effects of a change in TI are demonstrated in Figures 10.20a-d, showing a 1 cm thick transverse MIP reconstruction from the originally acquired coronal data set. Figure 10.20e shows the result for the syncopated 3D FLASH evaluation. The selection of TI to null out blood can be sometimes cumbersome as demonstrated in the examples of Figure 10.20. The signal from the superior vena cava (R_1), the ascending aorta (R_2), the main pulmonary artery (R_3) and the descending aorta (R_4) are evaluated from Figures 10.20a-d and plotted in Figure 10.21 to demonstrate the variability in the signal from blood as a function of the inversion time TI . Note that this variability can be expected from Figure 10.20e, which shows already brighter and darker blood in the different regions evaluated. The blood signal can be significantly suppressed as compared to fat, but it can introduce some ambiguities at the time the diagnosis is performed, especially when it is assumed that all the vessels are equally suppressed. This problem arises from the presence of blood spins with different states of saturation.

One solution to this problem can be attacked by exciting a larger volume covering the whole thoracic region and using higher excitation angles to quickly drive blood spins that only see the inversion pulse outside the imaging volume to rapidly reach equilibrium as they travel into the imaging region. Another solution to overcome these differences for blood is proposed in the following section with the use of an equalizer RF pulse.

Figure 10.19: 2 cm thick axial MIP reconstructions from an axial excite, coronal encoding sequence using a $TW=500$ ms (a,c) are compared to the same locations using the 3D IR-FLASH sequence with an inversion time of $TI=300$ ms and $TW=200$ ms (b,d). Note that the blood signal is not zeroed out but has been considerably suppressed as compared to shorter T_1 tissues. The arrows indicate regions of fatty tissue, exhibiting a short T_1 . Imaging parameters were: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z/N_x=64 \times 256$, $R_x=1.0$ mm, $R_z=1.6$ mm, $R_y=1.5$ mm and $N_{acq}=8$. The central lines of k -space were acquired using an asymmetric sequential data collection with $N_{off}=32$.

Figure 10.20: Signal behavior for 3D IR-FLASH as a function of TI with a fixed $TW=200$ ms and (a) $TI=10$ ms; (b) $TI=110$ ms; (c) $TI=210$ ms and (d) $TI=310$ ms. Note the difference in the signals from blood in the superior vena cava, main pulmonary artery and aorta. It is often seen that there is no single value of TI able to null out the blood signal in all compartments. The slab excited was 10 cm thick. (e) shows the case without the inversion pulse applied. Imaging parameters were: 3D IR-FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.0$ mm, $R_z=1.6$ mm, $R_y=1.5$ mm and $N_{acq}=8$. The central lines of k -space were acquired using a centric acquisition order with C_8 .

Figure 10.21: Signal from the superior vena cava (R_1), the ascending aorta (R_2), the main pulmonary artery (R_3) and the descending aorta (R_4) as a function of TI for a constant $TW=200$ ms. The signal from pericardial fat varied slightly between 794 units for $TI=10$ ms to 850 units for $TI=310$ ms, variation within the standard deviation of the measurement.

10.7 Equalizing the Magnetization Dynamics of Blood Spins

Even when all tissues are inverted by the 180° pulse, the evolution of the longitudinal magnetization can be very different for those spins inside the imaging slab as compared to those outside. This effect is dramatic for moving spins such as blood, as pointed out earlier in Figure 10.20, due to the fact that blood in different regions does not experience the same magnetization dynamics during the encoding process as a result of its motion during the acquisition. This means that the effective inversion time TI will be different for blood inside the imaging volume and it will be impossible to null the signal from blood completely with a single inversion time. Nevertheless, a risk can be taken by assuming that the timing parameters are chosen in such a way that for the worst condition, exemplified by having blood maximally refreshed during TI and TW , the inversion time and sampling flip angle are calculated so that at the branching of the main pulmonary arteries, the behavior for blood spins distally is the same because the system has achieved a “steady state” condition within the region of interest. Nevertheless this approach assumes that the physiology of all individuals studied is the same making the approach impractical in most cases due to the ambiguity in the choice of TI .

The plot of Figure 4.10 demonstrated the differences in the nulling time after the application of the inversion pulse for a blood spin during the first time is being excited by the string of α pulses to the time it reaches a steady-state. Even though Figure 4.10 has been simulated for the approach to equilibrium for stationary blood at the beginning of the 3D IR-FLASH acquisition, this process occurs dynamically during imaging since blood can be flowing into the imaging slab for the first time as compared to blood that has been within the excitation region for a longer period of time. This can also be seen by noting that the effective TW for spins outside the slab is the interval between the two inversion pulses as opposed to the TW defined between the last α pulse and the next inversion.

To equalize the zero crossing for all blood spins, all spins in the sample must be

subjected to the same train of RF pulses during the section select encoding. This can be accomplished by exciting the sample conveniently with two RF pulse trains defining two excitation regions during each repetition interval. One RF pulse defines the region of the slab from which signal will be encoded (sampling RF excitation, RF_s) while the other, defines the regions outside the imaging volume of interest (equalizer RF pulse, RF_e). This concept is illustrated in Figure 10.22. The imaging sequence is conveniently designed to produce signal from the former RF excitation while the spins excited with the latter RF, an equalizing RF pulse with the same effective flip angle as the sampling RF, are dephased (spoiled) to eliminate their contribution during the volume encoding and eliminate aliasing artifacts. The sequence diagram is demonstrated in Figure 10.23. It has the same structure as the axial excite, coronal read sequence but with the addition of the equalizer RF structure. The equalizing bands were chosen to have a constant thickness of 25 cm above and below the 14 cm excitation region. This thickness was selected given that if blood is assumed to flow at a speed of 40 cm/sec in the superior and inferior vena cava, for the $TI + TW$ combination of 400-600 ms usually employed, spins would reach the imaging volume already demonstrating the same longitudinal magnetization as those spins within the volume of interest at $\alpha=10^\circ$.

This sequence gave the expected results on volunteers, as demonstrated in Figures 10.24a-d, which compare the four different combinations possible that produce signal from the volume of interest. Figure 10.24a shows results equivalent to the syncopated 3D FLASH example collected by removing the inversion pulse and the equalizer RF pulse RF_e . Figure 10.24b includes the RF equalizer pulse in the syncopated FLASH acquisition of Figure 10.24a, and the blood signal in both chambers should have the same signal (disregarding coil sensitivity effects). The complete setup using the inversion and equalizer pulse to null out evenly the signal from blood, as shown in Figure 10.24d, confirms the previous statement for Figure 10.24b. Including the inversion pulse, blood is suppressed, as seen in Figure 10.24c, but it demonstrates clearly that $TI=240$ ms, calculated from the equilibrium conditions of Equation 4.14 for $TR=11.75$ ms, $\alpha=10^\circ$,

$TW=200$ ms, $N=128$, and 16 preparation RF pulses (C_{17}) for blood, can only null out the blood in the left ventricle, considered already at steady state conditions.

Figure 10.22: Saturation regions are placed above and below the imaging volume to equalize the behavior of blood spins within the volume and permit a single TI to null out the blood evenly in a 3D IR-FLASH experiment.

Figure 10.23: Sequence that equalizes the magnetization dynamics of blood inside and outside the imaging region to allow uniform blood signal suppression across the 3D volume. The sampling RF, RF_r , excites the volume and the signal is refocused. After the echo is read, the equalizing RF pulse, RF_e , is applied at the end of the sampling window to help drive the same magnetization behavior for spins outside the excitation volume.

Figure 10.24: Axial MPR reconstructions from a coronally acquired data set showing the effects of equalizing RF pulses outside the imaging volume to help suppress blood uniformly inside the imaging volume. (a) shows the results obtained by setting the IR pulse and the equalizing pulses to zero, similar to the standard syncopated 3D FLASH. (b) shows demonstrates the use of the equalizer RF pulse in (a) outside the imaging volume. Note that blood appears homogeneous in all the regions. (c) shows the effect of the IR pulse applied alone. Using the IR pulse in conjunction with the equalizer RF pulse, blood is homogeneously suppressed. Imaging parameters were: 3D IR-FLASH, $TR=11.75$ ms, $TE=2.5$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z/N_x=64 \times 256$, $R_x=1.10$ mm, $R_z=2.2$ mm, $R_y=1.5$ mm and $N_{acq}=5$. $TI=240$ ms and $TW=200$ ms with the central lines of k -space were acquired using a centric acquisition order with C_{17} .

10.8 The Effects of K-space Order on Blood Signal Suppression

Such as evaluated in Section 6.5.2, the response of 3D IR-FLASH with k -space ordering for tissue suppression is far from being ideal. The degree of suppression depends not only on the choice of TI and imaging parameters, but also on the size of the blood vessels (i.e., its spatial frequency) with respect to the FOV along which the encoding during the approach to equilibrium is taking place and the equilibrium value of the magnetization at the end of data collection for each in-plane phase encoding step.

The filtering effects are clearly demonstrated in Figure 10.25. To eliminate ambiguities arising from differential enhancement of blood at different equilibrium conditions, the sequence structure of Section 10.7 incorporate the equalizer RF pulse within the 3D IR-FLASH to even out the signal for blood. Using this sequence a relatively longer TR is employed, which allows for a higher steady state value at the end of the collection of all partitions as well as a shortening in the approach to equilibrium. This introduces, therefore, a slightly worse filtering response. Figure 10.25a demonstrates the results from a syncopated 3D FLASH acquisition intended to serve as a reference for the 3D IR-FLASH scan of Figure 10.25b to compare the position of the location of the small vessels at the periphery of the lung. Good blood suppression can be seen for blood in the aorta. Worse suppression is seen in the smaller blood vessels, as expected. Figures 10.25c,d show a more anterior coronal slice in the region of the vena cava, obtained with the same set of scans on another individual and demonstrating again the less ideal suppression of smaller vessels as compared to the signal in the vena cava, ascending aorta and pulmonary artery. The effectiveness of the suppression was evaluated by measuring the signal in several of the small vessels from both the syncopated 3D FLASH and 3D IR-FLASH scans (2-4 pixels across on the reconstructed image). Given the presence of the edge enhancement effects due to the highpass filter introduced, the small vessels in 3D IR-FLASH were suppressed between 2.5 to 3.5 times, well within the ranges expected, such as previously demonstrated in the simulations done on the

vessel resolution model in Figure 6.14.

Figure 10.25: High k -space filtering artifact with 3D IR-FLASH showing poor suppression for small blood vessels in the periphery of the lung. (a) shows the results from the syncopated 3D FLASH scan. (b) demonstrates good blood suppression in the aorta. Note that in the periphery of the lung the signal from small vessels is retained and correlates well with the vessels seen in (a). Images were formed by adding 4 1.5 mm thick slices from the coronal slices reconstructed along the region of interest in order to increase S/N. (c) and (d) show the same scans performed on another volunteer and displaying a more anterior coronal view, in the region of the vena cava, demonstrating once again the less ideal suppression of small vessels as seen in the right lung. Imaging parameters were: 3D IR-FLASH, $TR=11.75$ ms, $TE=2.5$ ms, $TI=240$ ms, $TW=200$ ms, $\alpha=10^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.10$ mm, $R_z=2.2$ mm, $R_y=1.5$ mm, $N_{acq}=5$ and C_{17} . The equalizer bands for blood were used for both to equalize the magnetization of blood in all the regions.

Similar results were obtained using the asymmetric sequential and cyclic data order for the same scan parameters ($TI=240$ ms and $TW=200$ ms with the center line collected during the 17th RF pulse, $N_{off}=17$). Slight differences between the scans were appreciated and they were mainly reflected in the signal of bigger structures, i.e. muscle. It was impossible to differentiate the effects on small vessels due to the low S/N and the more obvious effects of vessel blurring during the scan.

10.9 Syncopated FLASH and 3D IR-FLASH Studies in the Pulmonary Vasculature of Patients with Suspected Pulmonary Embolism

In this section, studies performed on several patients with different perfusion abnormalities on the ventilation/perfusion scans are compared with the syncopated 3D FLASH and 3D IR-FLASH scans obtained.

Pulmonary MR angiograms generated with the syncopated 3D FLASH acquisition were performed in all the patient population. The addition of the 3D IR-FLASH to the studies was determined at a later point during this work, direct consequence of the difficulty in verifying the findings in the pulmonary MR angiogram and the inadequate studies obtained, in many cases, due to the extensive blurring involved due to the uneven respiratory pattern of these patients (presenting dyspnea or, in some instances, highly hypoxic). For the latter, the number of studies is restricted and covers a small population of 11 patients. Nevertheless, results were far more interesting than those demonstrated previously by the syncopated 3D FLASH acquisition alone.

The first two selections shown are taken from those studies in which the pulmonary MR angiogram was the only study performed. The studies that follow afterwards demonstrate the utility of the 3D IR-FLASH to determine the presence of pulmonary embolism.

The case shown in Figures 10.26a-c presents several views of the reconstructed pulmonary MR angiogram of a patient with an indeterminate V/Q with a matched

abnormality in the lateral wall and base of the right lung. A nice depiction of the vasculature was possible in this case but it was certainly difficult to determine the presence of vessel cutoff or filling defects due to the presence of masses and pleural effusion surrounding the vessels. Note that even in this example where the thoracic wall was completely removed, the visualization of the vasculature is not complete from any of the angles shown. Review of the 3D data collected with MPR was helpful in that a questionable vessel going into the lateral mass observed could be tracked down to the point in which a sudden decrease in the vessel signal was observed. Nevertheless, it was difficult to correlate this with a vessel obstruction due to the similar intensities within the mass surrounding the site involved.

Figure 10.26: Pulmonary MR angiogram of a patient with suspected pulmonary embolism demonstrating 3 different MIP views. The V/Q scan showed a matching ventilation perfusion defect that corresponded to an infiltrate in the same location on chest X-ray. Four different MIP views of the arterial tree are shown, reconstructed from a sagittal excite, coronal readout scan. (a) lateral, (b) 66° sagittal towards coronal, (c) frontal. Imaging parameters: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=350$ ms, $\alpha=14^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.4$ mm, $R_z=1.05$ mm, $R_y=1.5$ mm and $N_{acq}=7$, Asymmetric sequential with $N_{off}=32$.

Abnormalities such as atelectasis, pleural effusion, infiltrates, or an elevated hemidiaphragm occur in the majority of patients with pulmonary embolism. Nevertheless, those patients with COPD (chronic obstructive pulmonary disease) present V/Q scans similar to those obtained in patients with pulmonary embolism in that wedge like perfusion abnormalities are visualized but that have nothing to do with a vascular obstruction caused by the settlement of clot.

Figure 10.27: A 64 year old patient with extensive gas trapping in the lung bases due to severe COPD. The MIP reconstruction of the pulmonary MRA shows marked pruning and irregularity in the right lung base, consistent with Bullous disease. Imaging parameters: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=350$ ms, $\alpha=14^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.6$ mm, $R_z=1.0$ mm, $R_y=1.56$ mm and $N_{acq}=7$, Asymmetric sequential with $N_{off}=32$.

Figure 10.27 shows an MIP reconstruction from a patient with an indeterminate V/Q

scan showing extensive gas trapping in the lung bases due to severe COPD, consistent with Bullous disease. Enhancement of the vasculature toward the apex of the lung is evident and seems to indicate the most well perfused region. The arterial tree to the lung base appears pruned and irregular just as would be expected on pulmonary contrast angiography, similar to the diagram shown in Figure 1.1d, characteristic of patients with hypertension. Also, the relatively low signal from these vessels suggests a low flow rate to the base. Note that veins are quite well demonstrated in this study and partially obscure the arteries.

The protocol used to evaluate patients varied according to the clinical history and the results of the V/Q scans. Patients with hypertension or congenital heart disease were only evaluated with the syncopated 3D FLASH scan alone. Knowing that the blood flow rates in these patients was lower than in normal volunteers, lower flip angles were used in order to reduce the saturation of blood and optimize its signal.

When patients were suspected with an indeterminate and high probability V/Q scan for pulmonary embolism, the 3D IR-FLASH sequence was added in order to provide the strong T_1 weighted scan to help distinguish clots from surrounding tissue and blood.

As pointed out previously, verification of the presence of pulmonary emboli was more consistent when both syncopated 3D FLASH and 3D IR-FLASH scans were combined, or just blindly using the results from the latter (which is convenient in cases where patients are not stable and the examination must be performed in the least time possible).

The following case shows a patient with an indeterminate V/Q scan presenting a broad perfusion defect in the left lung (Figure 10.28a) consistent with high probability for pulmonary embolism, and confirmed with a contrast angiogram study as shown in Figure 10.28b. The contrast angiogram demonstrates the presence of a mass blocking the left pulmonary arterial tree in its descending branch to the base as well as a small mass, partially occluding an artery going to the apex (arrows). Evaluation with the syncopated 3D FLASH scan was performed and a partial MIP view reconstructed in

the ROI to produce the pulmonary MR angiogram shown in Figure 10.28c. The latter failed in demonstrating signal voids in the regions of occlusion indicated in the contrast angiogram and the study was followed with the collection of the 3D IR-FLASH scan, the resulting MIP generated depicted in Figure 10.28d. Bright signal within the arterial lumen was detected in the regions of occlusion, indicative of possible clots.

(a)

(b)

Figure 10.28: Patient with a broad perfusion defect from the V/Q scan (a) in the left lung indicative of a severe vascular obstruction, presents a mass completely blocking the descending branch of the left pulmonary artery and partially blocking a branch towards the apex verified in the contrast angiogram (b) (arrows). The MR angiogram was performed (c) showing bright signal in the positions of expected signal void. Bright regions are seen after having suppressed the blood signal with the 3D IR-FLASH scan (arrows) (d). A weighted subtraction was performed by scaling the 3D IR-FLASH scan and subtracting it from the syncopated 3D FLASH scan to show only vascular information (d). The results from (e) can now be correlated with the contrast angiogram. 3 cm thick MIP's, slightly out from the frontal plane, were reconstructed in the region of interest. The branches at the base shown in (b) were not included during the MIP reprojection to avoid the interference from the thoracic wall. All scans collected with a sagittal excite, coronal readout sequence scheme. Imaging parameters for (c): syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=350$ ms, $\alpha=14^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.6$ mm, $R_z=1.0$ mm, $R_y=1.56$ mm and $N_{acq}=7$, C_{16} . For (d): 3D IR-FLASH with $TI=200$ ms / $TW=150$ ms / $\alpha=12^\circ$ / C_{16} , resolution as in (c).

Figure 10.28e shows a weighted subtraction obtained by scaling the resulting data from the 3D IR-FLASH scan and subtracting it from the syncopated 3D FLASH data before performing the MIP reprojection. The resulting image shows the signal voids that were expected in the regions of occlusion, even showing a thin bright line in the upper arterial branch demonstrating the partial occlusion of the vessel, correlating nicely with the contrast angiogram. Unfortunately, the scan was noisy due to the presence of spurious noise spikes in the data that deteriorated the quality of the study. Motion has also provided some image degradation in this case.

On the basis of this study, the first performed in the series with the 3D IR-FLASH scan included in the protocol, it is clearly shown the potential pitfalls of the syncopated 3D FLASH scan in the detection of clots. Note that in this case the clot appeared fairly isointense with the surrounding signal from blood. The isointensity can be justified since the location of the clot is proximal to the region of blood inflow with slightly diminished signal saturation from slow flowing spins. This is contrary to the case presented next, where clot, located distal to the site of fresh blood inflow, appears enhanced with respect to the blood signal in the vessel. Blood is assumed to have saturated completely before it was able to reach the location of the clot due to the short TR and relatively high flip angle used. Figure 10.29a demonstrates the location of two bright signal spots in the lower segmental branches of the right descending pulmonary artery (arrows). The bright signal that is seen surrounding the vasculature at the base arises from a hematoma and a bloody pleural effusion, later confirmed after drainage of the liquid buildup. The enhancement is an example of the paramagnetic relaxation enhancement mechanism during the oxidation states of blood that shortens the T_1 relaxation time due to the presence of large quantities of methemoglobin. (see Chapter 9). Figures 10.29b,c show two coronal slices from the originally reconstructed set of partitions from an axial excite, coronal readout 3D IR-FLASH scan in the region of the clots. Partial suppression of blood helps demonstrate the relation between the clots and blood vessels. This patient had an indeterminate V/Q scan showing a perfusion defect at the lower right lung base,

correlating once more with the findings from the MR study. The patient refused to have a contrast angiogram performed.

(a)

(b)

(c)

Figure 10.29: Patient study with a perfusion abnormality at the base of the right lung in the V/Q scan with high probability for pulmonary embolism. (a) shows the MR angiogram indicating two sites of abnormal enhancement in the segmental branches of the descending right pulmonary artery (arrows). (b) and (c) demonstrate two 1.5 mm thin slices from the original coronal data set from the axial excite, coronal read 3D IR-FLASH scan (arrows). Blood suppression was purposely set to suppress partially the blood signal. Imaging parameters for (a): syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=300$ ms, $\alpha=14^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=2.0$ mm, $R_z=1.0$ mm, $R_y=1.7$ mm and $N_{acq}=7$, C_8 . For (b) and (c): $TI=200$ ms / $TW=150$ ms / $\alpha=13^\circ$ / C_8 , with $TR=8.2$ ms, $TE=2.8$ ms, $N_y=128$, $N_z N_x = 64 \times 256$, $R_x=1.17$ mm, $R_y=1.56$ mm, $R_z=2.34$ mm and $N_{acq}=7$.

Patient follow up can be easily done with MR. During this study only two patients had extra sessions performed to evaluate the progression of the thrombolytic therapy. The initial results indicated the presence of clot in the 3D IR-FLASH scan but it was rather difficult to provide a concluding diagnosis based only on the MR angiogram, as described shortly. The inability to see abnormalities in the MR angiogram before and after treatment was more dramatic for the patient for which the data is not shown here, although multiple pulmonary emboli were clearly demonstrated during the first study and not in the follow up with the 3D IR-FLASH scan in the same region.

Figures 10.30a-f demonstrate the case of a patient with a perfusion defect in the right lung base as confirmed by the V/Q scan of Figure 10.30a, initially read as a high probability study for pulmonary embolism. Figure 10.30b depicts the results from a sagittal excite, coronal readout sequence acquired on the right lung and shows a sudden decrease in the signal of the descending pulmonary artery. An axial excite, coronal readout 3D IR-FLASH scan was performed, showing a brighter mass filling almost the entire vessel down to the base of the lung (Figure 10.30c). Blood suppression was poorly achieved in this case due to an incorrect choice of the sequence parameters. Figure 10.30d shows the 3D IR-FLASH scan performed after 2 weeks of anticoagulant therapy, demonstrating what it might be cataloged as blood clot retraction as the mass previously seen had collapsed into a smaller mass within the vessel lumen. Follow up after 1 1/2 months from the second examination, the 3D IR-FLASH scan showed

that the vessel had completely cleared out, demonstrating no abnormal signal intensity within the vessel lumen (Figure 10.30e). Figure 10.30f depicts the MR angiogram performed in this occasion, clearly showing a better enhancement of the vessel in the previously compromised region (see Figure 10.30b), indicating the reestablishment of blood flow to the lung base. Note that the quality of the MR angiogram of Figure 10.30f is slightly better than the previous study of Figure 10.30b, alluded to a more stable respiratory pattern (patient had dyspnea when first evaluated).

(a)

(b)

(c)

(d)

(e)

(f)

Figure 10.30: Pulmonary MR angiogram of a patient with suspected pulmonary embolism. The V/Q scan showed a matching ventilation perfusion defect at the base of the right lung (a). (b) shows the result of a sagittal excite, coronal readout scan performed on the right lung and demonstrating a sudden decrease in the signal intensity of the right descending branch of the pulmonary artery. (c) an MIP reconstruction from an axial excite, coronal readout scan demonstrates the presence of clot. The patient was treated with anticoagulant therapy and followed during another session to observe some dissolution of the clot (d). (e) shows complete dissolution of the clot 2 months after the onset of pulmonary embolism and treatment as the bright clot could not be identified. (f) shows the sagittal excite, coronal readout scan performed at this time demonstrating blood flow re-established towards the lung base. Imaging parameters for (b) and (f) were: syncopated 3D FLASH, $TR=8.2$ ms, $TE=2.8$ ms, $TW=350$ ms, $\alpha=14^\circ$, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=2.0$ mm, $R_z=1.0$ mm, $R_y=1.56$ mm and $N_{acq}=7$, C_8 . For the 3D IR-FLASH scans, (c) $TI=300$ ms / $TW=150$ ms / $\alpha=15^\circ$ / Asymmetric sequential with $N_{off}=32$. (d) $TI=200$ ms / $TW=250$ ms / $\alpha=13^\circ$ / C_8 (e) $TI=200$ ms / $TW=150$ ms / $\alpha=13^\circ$ / C_8 , with $TR=8.2$ ms, $TE=2.8$ ms, $N_y=128$, $N_z N_x=64 \times 256$, $R_x=1.17$ mm, $R_y=1.56$ mm, $R_z=2.34$ mm and $N_{acq}=7$.

The other patient that had the follow up performed had a similar outcome from the 3D IR-FLASH examination but the signal from blood was completely suppressed in this case. There were difficulties in appreciating the relationships between vessel and clot, demonstrating the utility of not having blood completely suppressed.

Table 10.3 summarizes the results obtained on 22 patients evaluated with the syncopated 3D FLASH scan. On the other hand, table 10.4 demonstrates the results from 11 patients that were also evaluated with the 3D IR-FLASH technique. These tables show the results from the V/Q scan evaluation on one axis and the diagnosis based on the MR scans on the other. A positive indication for pulmonary embolism in the syncopated 3D FLASH sequence was based on the observation of abrupt intensity changes along the arterial tree, and a negative indication if the opposite case applied. Scan exhibiting excessive blurring were cataloged as being inadequate to provide any diagnostic information. This simple classification criterion was sometimes difficult to apply, even in cases where good image quality was obtained. For the 3D IR-FLASH sequence, increased intensity within a suppressed vessel was indicative of the presence of a pulmonary embolus, and viceversa, a negative interpretation otherwise.

	low prob. V/Q	indeter. V/Q	high prob. V/Q
negative	2	6	3
positive		3	1
inadequate		4	3

Table 10.3: Results of the syncopated 3D FLASH technique in patients with suspected pulmonary embolism. A negative result was determined if no evidence of pulmonary emboli or vessel cutoff was observed. Positive results indicate that vessel cutoff or sudden drops in signal intensity along a vessel were seen. A scan was cataloged as inadequate if vessel blurring did not allow the clear visualization of third order branches.

	low prob. V/Q	indeter. V/Q	high prob. V/Q
negative	1	1	
positive		4	3
inadequate		2	

Table 10.4: Results of the 3D IR-FLASH technique in patients with suspected pulmonary embolism. A negative result indicates that no evidence of brighter signal from thrombus within the vessel was observed while positive results are confirmed in the opposite case. A scan was cataloged as inadequate if either blurring or poor blood suppression did not permit the visualization of bright clot signal.

It is important to note that TI , TW , centric ordering and number of RF/gradient pulses and flip angle varied slightly during the first studies performed with the 3D IR-FLASH technique (see imaging parameters in the 3D IR-FLASH examples of Figure 10.30). This was in part the reason for the failure of the two cases appearing as inadequate in Table 10.4, where the interpretation was difficult given that blood suppression was not good and the vessel signal remained comparable to that of fat.

The results on the eleven patients that were evaluated with both the syncopated 3D FLASH and 3D IR-FLASH techniques are shown together in Table 10.5 to corroborate the degree of confidence possible with either technique.

patient	sync FLASH	IR-FLASH	V/Q reading
1	-	-	low
2	-	-	indeterminate
3	+	+	
4	-	+	
5	+ ¹	+	
6	?	+	
7	?	?	
8	?	?	high
9	?	+	
10	+ ²	+	
11	?	+	

Table 10.5: Correlation between those patients having both the syncopated 3D FLASH and the 3D IR-FLASH scans performed. (-) indicates a negative scan for the detection of pulmonary emboli while (+) indicates a positive scan. (?) corresponds to cases in which scans were not adequate due to motion or bad blood suppression on the 3D IR-FLASH scans. The notes indicate: (¹)= clot appeared brighter than blood; (²)= no vessel cutoff with darker signal from clotted vessel.

The data of Table 10.5 suggests a correlation close to a 100% between the V/Q scan and the corresponding MR evaluation with the 3D IR-FLASH technique. This is certainly difficult to quote not having the contrast angiogram performed in all cases in order to demonstrate the correctness of the interpretation. In addition, it is noted that some uncertainty remains if the syncopated 3D FLASH scan is the only piece of information used for the diagnosis.

Chapter 11

Evaluation of the Pulmonary Vascular System with 3D MRI: Discussion and Conclusions

This chapter summarizes all the results and findings exposed in Chapter 10 during the evaluation of the pulmonary vascular tree using the syncopated 3D FLASH and 3D IR-FLASH techniques. The possibilities and drawbacks of both techniques in the evaluation of patients with suspected pulmonary emboli are discussed.

11.1 Vessel and Clot Visualization

11.1.1 Syncopated 3D FLASH

Arteries as well as veins can be visualized in both axially and sagittally excited scans. By using the sagittal excitation scheme, better inflow of fully magnetized spins can be achieved during the same delay time TW than in the axial excitation scheme. Arteries benefit from the inflow effects during TW while veins remain saturated, thus reducing vessel overlap and ambiguity problems. For this scheme, vessel blockage can then be better characterized. Nonetheless, care must be exercised in choosing TW so that the enhancement of the venous signal is such that arteries and veins begin showing similar intensities. For this scheme, vessel blockage can then be better characterized. It has been noted that the shorter T_1 of clot compares to the signal intensity of inflowing blood

in the 3D angiograms and makes distal clots hard to distinguish when inflow effects do not prevail. Section 10.9 shows, in fact, two blood clots that appeared brighter than surrounding in one patient in both of the tertiary branches of the descending right pulmonary artery (see the case of Figure 10.29). When using the axial excitation scheme, inflow enhancement is not enough to create major differences in the signals from the blood pool and clots and it is less optimal for the detection of pulmonary emboli.

11.1.2 3D IR-FLASH

Black blood imaging with SE sequences has demonstrated in the past excellent contrast to distinguish clot, further enhanced relative to blood due to its short T_1 (T_1 of the clot may vary depending on its age, see Chapter 9). The application of 3D IR-FLASH with TI chosen such that blood signal was reduced to accentuate the T_1 differences between clot and blood was found useful in discriminating clots within vessels in most patients. It is reasonable to believe from the data shown (see Tables 10.3 to 10.5) that the 3D IR-FLASH scan can be given an accuracy for the detection of pulmonary emboli close to 100%. This sequence can be thought as being a 3D substitute for the SE technique, with the advantage over the latter that slow moving blood will not be confused with clot and the resulting images benefit from 3D reformation as well.

Although the number of patients evaluated is not extensive, the 3D IR-FLASH reduced in most cases the signal from blood so that some vessel signal was still maintained while demonstrating bright clot and fat. A 3D suppressed angiogram was then reconstructed to show the clot position relative to the vessel. Examples are found in Figures 10.29 and 10.30. To date, the clot signal has been shown consistently brighter than the suppressed blood in 3D IR-FLASH although care must be taken since in the few studies done brighter and darker clots as well as different degrees of signal suppression in blood were seen. A distinctive feature that has been appreciated using the 3D IR-FLASH technique is that by having blood suppressed, the blurring due to motion only

affects the signal of possible clots within the vasculature. Even in cases where extensive motion existed, it was assumed that a positive clot detection was possible given that the signal in the region of the clot would, in all cases, be above the background noise level. Nevertheless, non-uniform blood suppression was noted in many of the volunteer cases evaluated such as demonstrated in Figure 10.20. This was seen as a potential factor for confusion during diagnosis in clinical cases. To provide a uniform suppression, an extra RF excitation was applied outside the volume of interest to equalize the behavior of all blood spins so that TI would be the same for all blood spins. The effect of the equalizer RF pulse was demonstrated in Figure 10.24. The slabs defined by the equalizer pulse perform their equalization function although there is a penalty involved in that heat deposition can be problematic in heavier individuals due to a three-fold increase in RF power applied (2 slabs are defined by a single RF and having assumed the same RF application times and gradients), and also a longer TR given that extra RF and gradient pulses are required for the equalization task (a 4 ms increase). Even though low flip angles are used, the short RF pulses applied in conjunction with larger gradients and thick volumes to better define the excitation profile increase the voltage of the RF pulses applied enormously.

Edge enhancement effects inherent to the acquisition during the approach to equilibrium must be also taken into account during the evaluation since small vessels are not suppressed completely and the remaining signal might contribute to false positives for the presence of a pulmonary embolus.

11.1.3 Using Motion Sensitive Scans

The sensitivity of the MR signal to the presence of motion was initially utilized to explore another avenue of differentiating clot from moving blood. A 3D double echo sequence encoding the ROAST and CE-ROAST signals simultaneously (FID and RF echo portions in a SSC experiment) was evaluated to achieve this goal. Nevertheless, this approach was rapidly abandoned since it was too sensitive to any motion present

within the chest wall. This sensitivity to motion was difficult to control but it was taken advantage of to produce a mask image of the thoracic cage to help remove the latter from the syncopated FLASH scans (see Section 11.7). The anteroposterior motion of the chest wall is small and transverse coherences can be maintained during the rapid string of RF pulses applied per in-plane phase encoding step. The liver, moving craniocaudally with the diaphragm, for example, presented a considerable amount of ghosting and signal loss due to the higher motion amplitudes present.

11.2 Sequence Parameters

11.2.1 Optimal Flip Angle

For a FLASH sequence during steady-state and considering stationary tissues, the optimal flip angle is given by the Ernst angle ($\alpha_E = \cos^{-1}(e^{-TR/T_1})$). The choice of flip angle for maximal signal for stationary blood for $TR=8.2$ ms is roughly 6.7° (assuming $T_{1\text{blood}}=1200$ ms). When flip angles between $7-10^\circ$ are used, the short TR and small flip angle still give an essentially T_1 weighted image. Brighter fat and clot are expected, while blood and muscle should have intermediate signal (see steady-state signals for these tissues in Figure 4.8 at the end of each RF string). Depending on the k -space trajectory chosen (refer to Sections 6.5 and 10.3.2), the optimal flip angle to improve S/N may be different from the Ernst angle and, indeed, higher, if the central k -space lines in the slice select direction are collected at the beginning of each in-plane phase encoding and the object extent along the encoding direction covers a specific portion of the FOV (for $TR=8.2$ ms and $\alpha=14^\circ$, the object has to be at least 1/5 of the FOV chosen in order to maintain the signal given by the central line collected). Variable flip angles can also be used to optimize the signal or even flatten the approach to equilibrium for a specific tissue [44]. Data collection during the approach to equilibrium for a syncopated 3D FLASH scan equalizes the intensities in practice and reflects an image which lacks contrast.

The axial excitation scheme was used to cover both lungs so that imaging time could

be kept short. Nevertheless, saturation for both arteries and veins, in addition to the use of low flip angles, makes the image exhibit little contrast.

A slightly higher flip angle can be used when there is more inflow or a thinner slab is used [70]. Nevertheless, this enhancement is dependent on the volume size and its location, as well as the heart rates of the subjects studied. Blood saturation effects were noted in patients with low cardiac output (i.e. hypertensive patients) for both axial and sagittal excitation schemes. In this case, the flip angle chosen was 7° for the axial excitation scheme.

The sagittal excitation has a better chance to show the differences between arteries and veins even in the case of slow flow. Assuming that sufficient blood can be refreshed during TW , arteries will show brighter than veins just considering saturation effects and the approach to equilibrium of freshly magnetized blood. Yet, it must be considered that the sagittal slab saturates part of the assumed fresh blood returning to the heart and blood enhancement is not as dominant as compared to the axial excitation scheme.

11.2.2 Centric Ordering

Centric ordering of the data during the approach to equilibrium plays a major role in the enhancement of the S/N and the optimal utilization of the inflow effects and magnetization recovery developed during TW . In the current implementation, the lack of a gradient preparatory stage to eliminate some of the eddy current effect was a problem, although considerable enhancement was still available by sparing some of the signal during the RF/gradient preparatory stage. Higher flip angles were not chosen so that the filtering effects over the data were not as dramatic, and at the same time allow for a better signal for the peripheral pulmonary vasculature in the cases where the blood signal did not benefit from the inflow effects during TW . The enhancement of small vessels using k -space ordering is not ideal in that for having an overall, good enhancement of those structures of different sizes contained in the FOV and avoid saturation effects, flip angles must be chosen close to the Ernst angle, or higher, knowing

a priori that inflow effects allow for its use so that the magnetization signal for most of the k -space lines have a more constant and higher signal values.

The benefits from having collected the signal during the approach to equilibrium and choosing a slightly longer TR with the same overall acquisition time seem to compete in this setup. Clear and consistent improvement was seen for centric ordering over a longer TR acquisition during the trials on the carotid arteries, as shown in Figure 7.17, but this was not obvious in the pulmonaries since a major portion of the pulmonary artery runs parallel to the excitation slab with slower blood flow than in the former case.

11.3 Motion Suppression Strategies

11.3.1 Pseudogating

Motion artifacts can be maximally reduced if data acquisition is synchronous with the motion source. Triggered data acquisition is applied routinely for cardiac studies by using the electrocardiogram signal as a triggering source. Respiratory gating can also be used but it has been seldomly applied due to the long imaging times involved when the respiratory periods are several seconds long. To overcome the lengthy acquisition times and allow for some respiratory compensation, some imagers have incorporated specialized data collection schemes using respiratory reordering such as ROPE (Respiratory Ordering of Phase Encoding) [75, 76] and COPE (Centrally Ordered Phase Encoding) [73], that do not lengthen the imaging time and help eliminate respiratory ghosting artifacts but do introduce a blurring function that reduces the resolution in the image depending on the amplitude of the motion.

Multiple acquisitions is another convenient method for ghost reduction that can also be used to improve S/N. When averaging is done for multiple acquisitions of the same data set, the ghosts can interfere destructively and, under certain conditions that depend exclusively on the choice of the imaging parameters with respect to the motion itself, can lead to complete ghost cancellation. When this is taken into account, ghost reduction can be accomplished for 2D or 3D scanning if the pseudogating concept is

adopted [72]. Pseudogating can provide reasonable results without the use of triggering or breathholding.

Pseudogating cancels out the ghosts by shifting them apart a distance such that each ghost ends up aliased exactly on the top of the original unghosted object. This condition is met for 2D imaging when the sequence timing is constrained so that TR is an integer multiple of the period of the motion divided by the number of acquisitions. This relation holds only if one phase encoding step is acquired per TR , and TR is chosen such that

$$TR = \frac{T_{motion}}{N_{acq}} \quad (11.1)$$

Reasonable performance and image quality can then be accomplished with short TR 3D scans with pseudogating. This implies that TR , the number of slices, N_{ss} , and the number of acquisitions are combined so that the resultant product is an integer multiple of the motion period. This implies that for 3D imaging, pseudogating will occur when

$$TR = \frac{T_{motion}}{N_{ss}N_{acq}} \quad (11.2)$$

A practical implementation of 3D techniques and pseudogating for imaging the thoracic region can be realized with the short TR 's used (5 - 9 ms). The time to phase encode 64 to 128 slices can occur in a fraction of the respiratory motion and, in effect, freeze the position of the thoracic cage for each in-plane phase encoding line acquired. The latter assumption may not hold completely for cardiac imaging since data acquisition time can still be comparable to the cardiac period (i.e. $N_{ss}=128$), yielding a blurred image of the heart but no ghost associated to it. This indicates that for a syncopated 3D FLASH acquisition the overall time between phase encoding steps, TR_{eff} , after all the partitions are acquired is drastically reduced and multiple acquisitions can still be acquired in a reasonable time. This in particular allows TR_{eff} to be selected, according to the previous discussion, such that

$$TR_{eff} = \frac{T_{motion}}{(N_{ss}TR + TW)N_{acq}} \quad (11.3)$$

follows the pseudogating concept accordingly and where T_{motion} is specifically related to the respiratory period. In the case of a 3D IR-FLASH scan, TR_{eff} can be taken as

$$TR_{eff} = \frac{T_{motion}}{(N_{ss}TR + TW + TI)N_{acq}} \quad (11.4)$$

The energy of the acquisition should be concentrated at the location at which the heart and the thoracic cage remain for the longest time. Assuming that the heart and thoracic cage motion are similar in that there is a period of rapid movement and a resting period, corresponding to the inspiratory and systolic phase, and the expiratory and diastolic phase, respectively, the latter two correspond to the portion of the cycle with the highest probability of simultaneous occurrence even with the cardiac and respiratory motion having a different time scale. The image more likely to be reconstructed corresponds to a heart in the diastolic phase and the respiratory cage in the expiratory phase. This likelihood will vary depending on the subject studied and will be related, for the most part, on the respiratory pattern. It is expected that the large number of acquisitions (5-8) performed help accomplish pseudogating without having to worry too much about the respiratory frequency of the individuals studied.

Since data acquisition is not synchronized with the respiratory or cardiac cycle, collection of the central Fourier lines for which it would be beneficial to collect data with maximum inflow effects (maximum inflow occurs at roughly 300 ms from the R wave) will not always happen. Averaging multiple acquisitions makes it possible to enhance the blood signal more uniformly since it makes it possible to sample enough that, at any given point in k -space, data may be collected during maximum blood refreshment. It was noted that by using the syncopated acquisition with cardiac triggering, the intensities in the vessels, particularly in the main pulmonary artery and primary branches, were not as uniform as in the case where no triggering was used with TW selected such to match closely both acquisition times. The latter showed, in 4 out of 6 volunteers evaluated, more uniformity in the main pulmonary arteries. The effects of averaging multiple acquisitions was previously shown with the experimental work on the flow

phantom shown in Section 7.5.2 with pulsatile flow. This example clearly demonstrated the effects of averaging multiple acquisitions on the signal uniformity along the tube (refer to Figure 7.16).

11.3.2 The Acquisition Loop Order

For a continuous acquisition such as done in the TOF angiographic sequences, long TR 's and relatively low flip angles are used to avoid saturation of blood spins far from the inflow edge of the slice, or running parallel to it. To accomplish pseudogating, the short TR 's used enhance the blood saturation, reason for choosing a syncopated excitation to reduce this problem by collecting data during the approach to equilibrium in conjunction with centric ordering: the use of short TR 's is rather dramatic for the reduction of the encoding time per phase encoding step. Several approaches have demonstrated the collection of 2D images with limited number of phase encoding steps and have proven that rapid 2D scanning can freeze the respiratory or cardiac motion for an instant [77, 78, 79]. Multiple averaging is done to enhance S/N.

Even for a short TR 3D sequence, it is very important to take into account the order in which data collection is performed for the same reasons that the concept of pseudogating was introduced in the earlier section and applied to collect the data on all the pulmonary vascular studies performed in Chapter 10.

The acquisition loop can be positioned inside or outside the slice select phase encoding loop. The order is not important if only one acquisition is performed. For the case in which the acquisition loop is inside, the effective TR will be increased proportionally to the number of acquisitions averaged while in the case of having the acquisition loop outside, the effective TR is kept the same and multiple acquisitions are done over each in-plane phase encoding line before averaging is done. In the latter case, the syncopated sequence had to be designed so that the acquisition loop occurred over the collection of the in-plane phase encoding lines (Figure 10.3c). This is a natural consequence of having a preparation period and TW included, allowing for

a pseudogated data collection. The experimental data in Section 10.4.2 indicates that the order in which a 3D data collection with multiple acquisitions should be done is by acquiring all the slice select phase encoding steps first and then perform the average over the number of acquisitions collected for each in-plane phase encoding step.

11.3.3 Effects of Lung Geometry and Respiratory Frequency and Amplitude

It was observed that the degree of success on healthy subjects, based on the visualization of at least 4th order branches of the pulmonary arterial tree in the MR angiograms, varied upon their physical buildup. The thinner subjects with longer lungs produced the best results while shorter and more corpulent subjects with shorter and wider lungs were less optimal. In the former population, vessels were oriented more craniocaudally, along the major axis of motion, and experienced to a lesser degree the effects of motion. In the latter population, vessels are more parallel to the diaphragm and liable to more blurring. For these two extreme cases, vessels toward the lung apex had the least blurring associated since they are oriented more craniocaudally and the motion amplitude is already significantly reduced in this region.

The 3D MR angiogram has demonstrated superior quality on volunteers and patients with low probability and indeterminate V/Q scans than those with high probability V/Q scans for the detection of pulmonary embolism or suffering hypertension. Subsecond imaging based on a very short TR (6 ms) 2D FLASH scan (collecting 64 to 128 lines along the in-plane phase encoding direction) was used to sample the respiratory waveform of several healthy individuals and patients. A sagittal orientation permitted to visualize both the movement of the diaphragm and the anterior chest wall. Most of the volunteers had a respiratory period from 3 to 5 sec, with the inspiratory period ranging from 1/4 to 1/3 of the respiratory interval. This indicates that for most of the time, data collection occurs during the expiratory period, for which the vessels move the least. The diaphragmatic excursion is similar in all the regions of the diaphragm with slightly less excursion anteriorly and increasing as it goes posteriorly, although it varies

between subjects. Vessel motion in the craniocaudal direction has been noted to be more or less proportional to the distance between the apex and the diaphragm (the apex is mostly stationary and the anteroposterior motion is usually several times smaller than the craniocaudal motion). In critical patients, the respiratory waveform was approximately sinusoidal and of higher frequency. The diaphragmatic motion is not uniform and sometimes erratic, and most of the excursion occurs posteriorly, making the vessels experience extensive motion craniocaudally as well as anteroposterior motion at the same time. Normal quiet breathing is accomplished almost entirely by the downward and upward movement of the diaphragm. An edge detector and cross correlation program was developed to track the motion of the diaphragm, vessels and chest wall to verify the motion patterns described above. A more detailed analysis on the effects of motion and pseudogating with multiple acquisitions has been explored [80] on a heart model subjected to different amplitudes and frequency of the respiratory motion, as well as the effect of the gating ratio and gating threshold on the resolution of the interfaces and coronary arteries. Some discussion on respiratory kinematics using MR has been recently reported [81].

By using multiple acquisitions, the respiratory motion is effectively pseudogated [72] (minimizing ghosting artifacts although blurring occurs depending on the effective displacement of the thoracic cavity and vessels). The respiratory frequency was not monitored to provide an estimate of the effective TR to be used for pseudogating. It was noted in volunteer studies that the variation of TW did not play a significant role in the vessel sharpness or the reduction of motion artifacts for a fixed number of acquisitions. Assuming that data collection for each in-plane phase encoding step is a fraction of the respiratory motion (true in normal volunteers), N_{acq} unghosted images at different points in the respiratory cycle are collected and, when averaged, as is automatically done by the system, gives a blurred image. The point spread function (PSF) can be estimated from the amount of blurring that occurs. Cardiac motion contributes as well to blur the vessels. Nevertheless, volunteer studies recorded with and without cardiac

triggering, but with respiratory gating, did not show dramatic differences in vessel sharpness. The predominant effect in blurring the vessel is the diaphragmatic motion during respiration.

Respiratory gating and cardiac triggering could alleviate much of the motion problem for 3D imaging. On volunteers, images acquired with and without respiratory gating and cardiac triggering are comparable. Imaging time is augmented with physiologic gating and less S/N per unit time is available. Nevertheless, it is expected to be important for clinical studies due to the complex motion in critical patients. Doubling the short scanning times being used for pulmonary imaging is not prohibitive if good image quality is obtained. The shorter respiratory period of patients should aid in achieving shorter scanning times, especially if better surface coils become available to help boost the S/N. Some work has been done in acquiring 3D scan with much lower resolution with cardiac triggering in 32 heart beats and breatholding [82].

11.3.4 Reproducibility

A controlled study to assess the reproducibility of both the syncopated 3D FLASH and 3D IR-FLASH techniques was not performed as such with a protocol in which all imaging parameters were kept the same during a finite number of sessions. A retrospective evaluation on some individuals that underwent several studies, demonstrated that 4th to 6th order branches were visualized consistently on all scans evaluated, particularly in the vessels of the lung apex. It has to be taken into account that blurring affected vessel sharpness, and the quantification of the size and intensities observed was difficult, especially when the vessel is not found at the same location. Vessels down to the size of a pixel in-plane (1.2-1.8 mm diameter for $R_z=0.8$ mm and $R_y=1.5$ mm) could be visualized, and which corresponded to 5th and 6th order branch vessels. This was the case on one volunteer in which 12 different scans were performed and similar MIP views were reconstructed.

Scan reproducibility was noted in the two patients that had follow up sessions after

therapy. The case shown in Figures 10.30b,f demonstrates the detrimental effects of motion before and after the thrombolytic therapy was performed to dissolve an embolus in the right descending pulmonary artery. This indicates that if the respiratory pattern is stable during all sessions, which is the case for most volunteers, the resulting scans will be similar.

11.4 Realistic RF profiles

Ideally, the RF profile across the imaging volume should be uniform in order to provide the same tissue contrast for all the partitions collected. Nevertheless, the limitations on the RF power deposited on the patient, gradient strength and the need for short echo times, provided a trapezoidal like profile for the RF excitation. An example simulated profile was shown in Figure 7.5a, similar to the profile acquired for a 14 cm thick slab using a 640 μsec RF time applied in the presence of a 2 mT/m gradient that was used in all human studies involving the evaluations done on the pulmonary tree.

The gaussian shape is not far from being a good excitation profile for the sequence design implemented. For the axial excite coronal readout scheme, the sites of inflow occur perpendicular to the excited volume through the superior and inferior vena cava. Inflowing spins start experiencing a lower flip angle excitation at the entrance to the slab when blood is completely magnetized and saturate the spins traveling towards the middle of the volume to a lesser extent. This makes it possible to have a more homogeneous enhancement of the vessel along its pathway when blood is directed to feed the pulmonary arteries. For the sagittal excitation scheme, inflow is also perpendicular to the excited volume but in this case blood flows into each lung through the main pulmonary arteries.

The use of a ramped slice profile, such as demonstrated in the simulations of Figure 7.6, can be used to optimize the approach to equilibrium for inflowing blood and also the signal homogeneity of the vessel along the excited volume for standard angiographic sequences. This has been recently demonstrated with the use of TONE

pulses [50].

A gaussian excitation is more questionable when a 3D IR-FLASH sequence is used. The graph depicted in Figure 4.12 displays the variation of TI versus TW for a fixed flip angle. Since TI is calculated so that blood has a zero crossing during the collection of the central Fourier line for a fixed angle, a variation in the flip angle across the profile will give an inconsistency in the crossing through zero for blood. This variation is demonstrated in Figure 4.13 for $TW=300$ ms and a flip angle variation from 2° to 15° . It must be also considered that blood is not stationary, and it will experience different excitation angles while it moves into or through the imaging volume. An average TI can only be calculated depending on the direction of the blood flow with respect to the excitation profile. Disregarding RF profile effects, the TI for nulling out blood is longer for those spins that do not experience the RF defining the imaging slab than those remaining within the imaging volume. To equalize the behavior of blood spins, better RF profiles and extra RF pulses utilized for moving spins such as demonstrated and discussed in Sections 10.7 and 11.1.

11.5 Short Echo Times

Short echo times can be achieved using an asymmetric echo [70]. The data can then be reconstructed using specialized reconstruction techniques such as half Fourier, Constrained Reconstruction (CORE) and other reconstruction methods to recover the resolution loss such as seen in the half Fourier reconstruction example of Figure 10.18 [83, 74, 84]. The short echo time keeps both T_2^* signal loss in the vicinity of the lungs [24, 85, 86] and the effects of spin dephasing for moving blood small. The effects of T_2^* on the lung parenchyma were studied by varying the echo time of the sequences implemented from $TE=2$ ms to $TE=4$ ms and fitting the data to an exponential decay with a least square error approach. The values observed ranged between 3.5 ms to 12 ms depending on the region of the lung evaluated, with the longer echo times observed in locations close to the lung base and more posteriorly in the supine position (more

dependent zone with higher blood to air volume). Little perfusion is present in the least dependent areas (towards the anterior chest wall and apex). Progressive recruitment and dilatation of the capillary bed towards the bases causes the ratio of blood to interstitial fluid and lung tissue to increase, altering the relaxation properties of lung (T_2 as well as T_1). The echo time used, ranging from 2-3 ms, the signal from fat/water interfaces is reduced. This provides a better boundary definition between the vessels and the surrounding muscle and fat. At 1.5T, the first cancellation of water and fat signal occurs roughly at $TE=2.3$ ms, within the TE range used in these experiments.

11.6 Signal-to-Noise and Acquisition Times

Images are typically collected using a quadrature body coil. When high resolution studies are to be performed, even for 3D data collection, the body coil does not provide good S/N. A direct solution to augment the S/N is the use of multiple acquisitions at the expense of increased imaging time. A Helmholtz body pair or a phased array surface coil can also be utilized. The use of the latter coils will depend on the size and condition of the individual studied. It must be remembered that the reception of surface coils is not homogeneous and this can compromise the information at locations far from the coil (i.e., central pulmonary arteries).

In the current sequence setup, the fact that a reduced FOV and small number of phase encoding steps (N) are used to provide a desired resolution will lead to a loss in S/N proportional to the square root of the ratios of the number of phase encoding steps selected between comparable scans (N_1 and N_2 respectively). This is recovered, however, because N_{acq} is set to be N_1/N_2 , which regains the $N_{acq}^{1/2}$ in lost S/N. Total acquisition time is $N_{acq}N_yTR_{eff}$ which, for $N_{acq}=6$, $N_z=64$, $N_y=128$, $TR=8.2$ ms and $TW=500$ ms is approximately 10 minutes.

Breathhold and cardiac triggered 2D scans can be obtained with a surface phased array coil [87]. The availability of surface phased array coils is limited and, in practice, body coil images cannot be used for diagnosis for 2D imaging with high resolution due

to their very poor S/N . The collection of multiple 2D slices during one breathhold can be replaced by a cardiac gated breathhold 3D scan using reduced FOV and number of phase encoding lines. The 3D scans use ultrashort TR to augment the S/N with centric k -space ordering and $N_{ss}^{1/2}$, as well as short TE to reduce susceptibility artifacts and allow for contiguous slices. Physicians are interested in viewing only the arterial tree and a short 3D scan can saturate more efficiently the venous blood and enhance the arterial tree.

11.7 Image post-processing

Manual segmentation of the thoracic wall is usually performed to demonstrate the complete pulmonary vascular tree. An attempt for an automatic segmentation of the thorax was done by creating a binary mask using a flow sensitive 3D syncopated CE-ROAST acquisition that multiplied the resulting angiographic images.

A combined ROAST/CE-ROAST acquisition can be used to acquire two data sets simultaneously exhibiting completely different behaviors when motion is present. Figure 11.1a,b show 2 cm transverse MIP reconstructions from the coronally acquired data set showing the ROAST and CE-ROAST portion of the acquisition, respectively. The signal from blood, liver and heart remains in the ROAST acquisition but it has essentially a FLASH behavior. Signal remaining in the CE-ROAST scan is indicative of tissues that do not move significantly during the short acquisition time used to encode all partitions. The CE-ROAST image can then be used as a mask to eliminate unwanted tissue from the ROAST acquisition, such as the spine and the thoracic wall, before continuing further image processing. This idea is demonstrated in Figure 11.2 and applied to a data set acquired with the syncopated FLASH scan. Figure 11.2a shows one slice of the 3D FLASH syncopated acquisition. The corresponding CE-ROAST slice and the binary mask created are shown in Figure 11.2b,c. Figure 11.2d depicts

Figure 11.2a after being multiplied by Figure 11.2c.

Figure 11.1: Using the syncopated acquisition with a sequence structure containing both ROAST and CE-ROAST gradient waveforms makes it possible to acquire two data sets, one corresponding to the FID (a) and the other to the RF echo (b) components, respectively. The images show a 2 cm transverse MIP reconstruction from the coronally acquired data set. The high sensitivity of the CE-ROAST signal to motion demonstrates that moving tissue can be naturally eliminated, such as seen in (b) where the signal from heart and vessels is not shown. This approach demonstrates that even in the case that all the slice select phase encoding steps are acquired in roughly 680 ms, significant motion is present that destroys the SSC equilibrium in these structures. High flip angles are used to provide enough signal for the RF echo portion. Imaging parameters: $TR=10.5$ ms, $TE^+=2.6$ ms and $TE^-=2.9$ ms, $TW=500$ ms, $\alpha=20^\circ$, $N_z N_x=64 \times 256$, $N_y=64$, $R_x=1.2$ mm, $R_z=2.34$ mm, $R_y=2.0$ mm, $N_y=64$ and $N_{acq}=8$.

Figure 11.3a demonstrates the resulting MIP projection generated from the same data set after using the CE-ROAST mask to eliminate the thoracic wall. An MIP from the manually segmented data set is shown for comparison in Figure 11.3b. segmentation. The use of CE-ROAST to maintain the signal from tissues such as the heart and liver is nearly impossible due to their motion. For this reason, the mask does not eliminate them from the ROAST or FLASH images. This is not as troublesome for the right lung as it is for the left, where the heart obscures most of the vasculature.

Figure 11.2: The sensitivity to motion of a CE-ROAST sequence is used to create a binary mask to eliminate the thoracic wall. (a) demonstrates a slice acquired with a sagittal excite scheme using FLASH and the corresponding slice using CE-ROAST (b). (c) is a binary mask created from (b) that multiplies (a) in order to create (d). This is a natural way to eliminate the thoracic wall and avoid the manual segmentation of each slice before the MIP reconstruction.

Figure 11.3: MIP projections generated from the same data set after using a CE-ROAST mask to eliminate the thoracic wall (a), and manual segmentation (b). The use of CE-ROAST to maintain tissues such as the heart and liver is nearly impossible due to their motion. For this reason, the mask does not eliminate them from the FLASH images. This is not as troublesome for the right lung as it is for the left, where the heart obscures most of the vasculature.

Chapter 12

Conclusions and Future Directions

The evaluation of high resolution, short TR/TE 3D GE techniques without respiratory gating, cardiac triggering or breatholding has demonstrated that good quality pulmonary MR angiograms can be acquired in reasonable imaging times (8-13 minutes) with sufficient S/N and resolution to visualize up to the 5th and 6th branch order in the pulmonary arterial tree.

The visualization of the pulmonary vasculature with angiographic like techniques is still under evaluation today in both 2D and 3D modalities. The 3D approach taken here represents the initial trials in the application of 3D techniques based on k -space reordering during the approach to equilibrium of flowing blood. In this work, the syncopated FLASH acquisition is claimed to produce better results than TOF techniques in enhancing the pulmonary vasculature. The introduction of a wait time between in-plane phase encoding steps prior to the slice select phase encoding period permits a better manipulation of the enhancement possible for very short TR imaging given that an optimal k -space data collection pattern is chosen.

MR pulmonary angiography is still in its infancy and further refinements are yet to be seen in order to demonstrate its usefulness in disease discrimination and diagnosis. It is yet somewhat difficult to interpret the results obtained without the help of other imaging modalities and predict the extent of its practical use and confidence factor. It was found that the use of the 3D IR-FLASH technique was crucial in the determination

of pulmonary emboli in patients with indeterminate and high probability V/Q scans, and it is thought to provide a successful rate for the detection of the disease close to 100%. The 3D IR-FLASH technique demonstrated the failure of the syncopated 3D FLASH technique to show clots as signal voids, as initially thought to compare with the views generated in the standard contrast angiograms. The failure was attributed to the slower blood velocities in occluded blood vessels and in cases of hypertension which caused significant blood saturation, especially with the short TR 's and relatively high flip angles used. Another drawback is the fact that clots have, in general, shorter T_1 values than blood (depending on its age) which makes the signal gained during inflow to compete with the brighter signal from clot, as confirmed in one of the patients evaluated.

Tagging techniques such as SPAMM [54] and other interferometric methods have proven useful in the detection of pulmonary emboli. Phase images can also be used to differentiate moving material from stationary clot. The possibility of fatty tissue and clot being mistaken can be also ruled out by using the phase information in a syncopated 3D FLASH or 3D IR-FLASH scan. In occasions, pulmonary emboli can also arise from fatty tissue that has migrated from a traumatized or infected breast or from an injury to the marrow of the large bone structures after fracture, adding a source of confusion.

The 3D nature of the scans performed and the nearly isotropic data sets collected allow a multitude of post-processing possibilities. Data reformation in any orientation using multiplanar reconstructions (MPR), maximum intensity projections (MIP) or the application of vessel tracking algorithms to isolate a vessel of interest are some of the tools available to improve the visualization and diagnosis. Vessel tracking algorithms may become helpful for angiographic studies performed with the axial excitation coronal readout scheme. These studies show extensive anatomical information but the MIP projections are hard to interpret due to the extensive vessel overlap and lack of contrast between arteries and veins. Local or targeted MIP evaluation as well as segmentation algorithms to remove the thorax and the heart will be extremely helpful to remove obscuring features and reveal better the 3D information.

Another alternative, not addressed in this work, is the blood enhancement possible with intravascular contrast agents, such as Gd-DTPA. Contrast agents can reduce the T_1 relaxation of blood considerably and allow for maximum vessel enhancement, virtually independent from inflow effects. The use of contrast agents to enhance the pulmonary vasculature has been recently done using 2D and 3D techniques with continuous contrast injection and large flip angles during breatholding in order to avoid blurring effects from respiratory motion. Higher flip angles can be used as a result of the higher concentration of the contrast agent in blood before redistribution in the body. From a theoretical point of view, for the longer scans discussed in this work, data collection during the first minutes after contrast injection can be taken advantage of by choosing centric ordered acquisitions.

To maintain the resolution initially desired, the region of interest from which data collection is taking place should maintain its position during the length of the imaging period. If motion is present, the speed of data collection can play an important role in the resolution of the reconstructed image, such as in photography, where acquisition speed relative to the motion of the region of interest is of importance to maintain the sharpness in the final image. MRI has not yet matured to the point where highly resolved scans with adequate S/N can be acquired in a single shot. This is a direct consequence of the phase encoding process used in Fourier Transform NMR, the insensitivity of the NMR experiment and the physical restrictions inherent to the data acquisition hardware.

The speed of image acquisition is associated with the S/N, resolution and the particular phase encoding process used to acquire the final image. Scanning times are not instantaneous and it is unfortunate that for 3D imaging, in particular, the time needed to encode all the data can be long and the quality of the final images can be majorly degraded with motion occurring between different phase encoding views. This is of major concern since the thoracic region undergoes constant motion during the acquisition process. The problem of motion is more accentuated in patients. Patients with more extensive central pulmonary emboli are often clinically unstable. They are sometimes

on ventilators and in extreme hypoxic state when lying supine, which is the only possible position for imaging. Respiratory gating in conjunction with cardiac triggering has depicted, in many occasions, very high resolution images of the peripheral pulmonary vasculature using SE scans. This is possible because the acquisition is in synchrony with the motion and virtually removes the respiratory and cardiac blurring effects from the reconstructed images. The few attempts in using physiological imaging with 3D scans did not show any noticeable improvement in vessel definition as compared to the "free running" syncopated FLASH technique. This does not preclude the fact that motion monitoring might play an important role in the success of 3D imaging in the near future, when higher resolution and clinical reliability become the major issues to be addressed.

The sensitivity and reproducibility of the 3D approach taken here needs yet to be completely established. Nevertheless, the results obtained are certainly encouraging to further develop the use of 3D pulmonary MRI techniques and prove their usefulness in the evaluation of a wide variety of pulmonary disorders.

Surface coils are expected to play an important role for imaging in the thoracic region to increase the S/N (at least peripherally). The improvement in S/N would allow acquisition times to be kept short so that even sick patients, who often breathe rapidly, are unable to hold their breath, are in pain or have trouble keeping still, can be imaged successfully and quickly. Good image quality has been recently acquired using surface array coils, demonstrating that good S/N and high in-plane resolution with thick slices (8 mm) can be achieved using ultrashort TR 2D scans that can cover one whole lung in a single breathhold period. This can be easily extended to 3D imaging as well.

We foresee that major improvements in hardware and software in the near future will allow highly resolved 3D data sets to be acquired in the thoracic region with little image degradation due to respiratory motion, cardiac motion and moving blood. More flexibility in the software will make it possible to integrate new data collection schemes and reconstruction algorithms into the system. Introduction of higher gradient strengths,

reduced switching times, higher sampling rates and better coils will help achieve shorter echo times that translate directly into a considerable reduction of susceptibility artifacts and intravoxel dephasing in 3D GE imaging, while also allowing an overall reduction in imaging times.

Appendix A

Solutions to the Bloch Equations

The phenomenological equations of Bloch adequately describe the behavior of the bulk magnetization vector $\vec{M}$ of a sample immersed in a static and homogeneous field B_0 along the z axis, undergoing interactions with other external electromagnetic fields. During the application of an RF pulse along the x axis with amplitude B_1 and oscillating frequency ω_{rf} , the Bloch equations become in a rotating frame of reference at ω_{rf}

$$\frac{\partial \vec{M}}{\partial t} = \gamma \vec{M} \times \vec{B}_{eff} - (M_x \hat{i} + M_y \hat{j})/T_2 - (M_z - M_0)\hat{k}/T_1 \quad (\text{A.1})$$

where $\vec{B}_{eff} = (B_0 - \frac{\omega_{rf}}{\gamma})\hat{k} + B_1\hat{i}$ and T_1 , T_2 and M_0 represent the spin-lattice relaxation, spin-spin relaxation and the magnetization at thermal equilibrium, respectively. Separating Equation A.1 into its three components

$$\begin{aligned} \frac{\partial M_x}{\partial t} &= \delta\omega M_y - \frac{M_x}{T_2} \\ \frac{\partial M_y}{\partial t} &= -\delta\omega M_x + \gamma B_1 M_z - \frac{M_y}{T_2} \\ \frac{\partial M_z}{\partial t} &= -\gamma B_1 M_y + \frac{M_0 - M_z}{T_1} \end{aligned} \quad (\text{A.2})$$

where $\delta\omega$ is the offset from the resonance frequency ω_0 . The right hand side of Equation A.2 describes the free precession period, the effect of the B_1 field and the relaxation mechanisms that affect the net magnetization vector and can be used to solve

the dynamics of the magnetization during the application of the RF and the precession interval between RF pulses.

A.0.1 Magnetization Dynamics During the Application of the B_1 field

During the time the B_1 field is applied, the relaxation times T_1 and T_2 must not be important when compared to the precession about B_1 during τ_p : $\tau_p \ll T_2 < T_1$. The requirement on B_1 is given by [88]

$$\gamma B_1 \gg \frac{\pi}{2T_2} \quad (\text{A.3})$$

which also indicates that B_1 must be much larger than the internal fields or external field inhomogeneities described by T_2 . Considering $\delta\omega \ll \gamma B_1$ and the relaxation times negligible, Equation A.2 becomes

$$\begin{aligned} \frac{\partial M_x}{\partial t} &= 0 \\ \frac{\partial M_y}{\partial t} &= \gamma B_1 M_z \\ \frac{\partial M_z}{\partial t} &= -\gamma B_1 M_y \end{aligned} \quad (\text{A.4})$$

By solving Equations A.4 the magnetization immediately after the RF which rotates the magnetization towards the transverse plane by an angle $\alpha = \gamma B_1 \tau_p$, $\vec{M}^+ = (M_x^+, M_y^+, M_z^+)$, is related to the magnetization prior to the RF pulse, $\vec{M}^- = (M_x^-, M_y^-, M_z^-)$ by

$$\begin{aligned} M_x^+ &= M_x^- \\ M_y^+ &= M_y^- \cos \alpha + M_z^- \sin \alpha \\ M_z^+ &= -M_y^- \sin \alpha + M_z^- \cos \alpha \end{aligned} \quad (\text{A.5})$$

and introducing the rotation operator $\vec{P}_x(\alpha)$, where

$$\vec{P}_x(\alpha) = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos \alpha & \sin \alpha \\ 0 & -\sin \alpha & \cos \alpha \end{bmatrix}$$

Equations A.5 can be written in matrix form as

$$\vec{M}^+ = \vec{P}_x(\alpha)\vec{M}^- \quad (\text{A.6})$$

A.0.2 Magnetization Dynamics Between RF Pulses

In the absence of RF excitation, B_{eff} reduces to $(B_o - \frac{\omega_r t}{\gamma})\hat{k}$ and Equations A.7 drive the behavior of the transverse and longitudinal magnetization. Thus, the equations that must be solved are

$$\begin{aligned} \frac{\partial M_x}{\partial t} &= \delta\omega M_y - \frac{M_x}{T_2} \\ \frac{\partial M_y}{\partial t} &= -\delta\omega M_x - \frac{M_y}{T_2} \\ \frac{\partial M_z}{\partial t} &= +\frac{M_o - M_z}{T_1} \end{aligned} \quad (\text{A.7})$$

$\delta\omega$ demonstrates the analogous case where spins located in regions of magnetic inhomogeneity precess at a frequency $\omega' = \omega_o \pm \delta\omega$. $\delta\omega$ also arises if the spins were excited with an RF of slightly different frequency than ω_o . The solution to this situation yields

$$\begin{aligned} M_x(t) &= [M_x^+ \cos \beta(t) + M_y^+ \sin \beta(t)]e^{-t/T_2} \\ M_y(t) &= [-M_x^+ \sin \beta(t) + M_y^+ \cos \beta(t)]e^{-t/T_2} \\ M_z(t) &= M_z^+ e^{-t/T_1} + M_o(1 - e^{-t/T_1}) \end{aligned} \quad (\text{A.8})$$

with $\beta(t) = \delta\omega t$. Introducing the rotation operator $\vec{R}_z(\beta(t))$ and the operator $\vec{S}(t)$, Equations A.8 in matrix notation can be rewritten as

$$\vec{M}(t) = \vec{R}_z(\beta(t))\vec{S}(t)\vec{M}^+ + M_o(1 - E1(t))\hat{k} \quad (\text{A.9})$$

with the operators $\vec{R}_z(\beta(t))$ and $\vec{S}(t)$ defined as

$$\vec{R}_z(\beta(t)) = \begin{bmatrix} \cos \beta(t) & \sin \beta(t) & 0 \\ -\sin \beta(t) & \cos \beta(t) & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$$\vec{S}(t) = \begin{bmatrix} E2(t) & 0 & 0 \\ 0 & E2(t) & 0 \\ 0 & 0 & E1(t) \end{bmatrix}$$

where $E1(t) = e^{-t/T_1}$ and $E2(t) = e^{-t/T_2}$. The term $\beta(t)$, indicating the precessional angle that spins may undergo after the RF is applied, can be completely specified when the imaging gradients are present as

$$\beta(t) = \gamma[\Delta B_f t + x \int_{t_x}^{t_x} G_x(t) dt + y \int_{t_y}^{t_y} G_y(t) dt + z \int_{t_z}^{t_z} G_z(t) dt] \quad (\text{A.10})$$

where the limits of integration indicate the time periods of gradient application for the x , y and z axes, respectively and ΔB_f contains all the inhomogeneities present in the main magnetic field.

Appendix B

Solution of the Bloch Equations During Steady-State

Appendix A derived the motion of the magnetization during the RF application and the precession period and magnetization recovery and decay followed the application of the latter. Suppose that the RF excitation process is repeated several times with a constant interval between RF excitations denoted by TR, the repeat time. The magnetization immediately after the n th RF, $\vec{M}_n^+ = (M_{xn}^+, M_{yn}^+, M_{zn}^+)$, is related to the magnetization prior to the RF pulse, $\vec{M}_n^- = (M_{xn}^-, M_{yn}^-, M_{zn}^-)$, through the rotation operator $\vec{P}_x(\tau_p)$,

$$\vec{M}_n^+ = \vec{P}_x(\alpha)\vec{M}_n^- \quad (\text{B.1})$$

for a B_1 field applied along the x axis. Between RF pulses the magnetization vector behaves as described by Equation A.9. At the end of the precession interval, $t=TR$, the magnetization vector is given by

$$\vec{M}_{n+1}^- = \vec{R}_z(\beta)\vec{S}(TR)\vec{M}_n^+ + M_o(1 - E1)\hat{k} \quad (\text{B.2})$$

with the operators $\vec{R}_z(\beta)$ and $\vec{S}(TR)$ defined as

$$\vec{R}_z(\beta) = \begin{bmatrix} \cos \beta & \sin \beta & 0 \\ -\sin \beta & \cos \beta & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$$\vec{S}(TR) = \begin{bmatrix} E2 & 0 & 0 \\ 0 & E2 & 0 \\ 0 & 0 & E1 \end{bmatrix}$$

where $\beta = \beta(TR)$ (Equation A.10, $E1=e^{-TR/T_1}$ and $E2=e^{-TR/T_2}$). The magnetization vector following the next excitation pulse, $\vec{M}_{n+1}^+$, is related again to the magnetization prior to the RF pulse, $\vec{M}_{n+1}^-$, through the rotation matrix $\vec{P}_x(\alpha)$

$$\vec{M}_{n+1}^+ = \vec{P}_x(\alpha)\vec{M}_{n+1}^- \quad (\text{B.3})$$

$$\vec{M}_{n+1}^+ = \vec{P}_x(\alpha)[\vec{R}_z(\beta)\vec{S}(TR)\vec{M}_n^+ + M_o(1 - E1)\hat{k}] \quad (\text{B.4})$$

After a steady-state behavior is reached, the behavior of the magnetization vector is the same for all cycles of the RF excitation. This permits to calculate the steady-state magnetization by setting indifferently

$$\vec{M}_{n+1}^+ = \vec{M}_n^+ \quad (\text{B.5})$$

$$\vec{M}_{n+1}^- = \vec{M}_n^- \quad (\text{B.6})$$

Solving for these two separate conditions, the steady-state solutions for the magnetization prior to the RF pulse, $\vec{M}^-=(M_x^-, M_y^-, M_z^-)$, and after, $\vec{M}^+=(M_x^+, M_y^+, M_z^+)$, are given by

$$\vec{M}^- = M_o(1 - E1)[1 - \vec{R}_z(\beta)\vec{S}(TR)\vec{P}_x(\alpha)]^{-1}\hat{k} \quad (\text{B.7})$$

$$\vec{M}^+ = M_o(1 - E1)[\vec{P}_x(\alpha)^{-1} - \vec{R}_z(\beta)\vec{S}(TR)]^{-1}\hat{k} \quad (\text{B.8})$$

which written for each component

$$M_x^+ = DE2 \sin \alpha \sin \beta \quad (\text{B.9})$$

$$M_y^+ = D \sin \alpha (1 - E2 \cos \beta) \quad (\text{B.10})$$

$$M_z^+ = D(E2(E2 - \cos \beta) + \cos \alpha)(1 - E2 \cos \beta) \quad (\text{B.11})$$

$$M_x^- = M_x^+ \quad (\text{B.12})$$

$$M_y^- = -D \sin \alpha E2(E2 - \cos \beta) \quad (\text{B.13})$$

$$M_z^- = D(1 - E2 \cos \beta - E2 \cos \alpha(\cos \beta - E2)) \quad (\text{B.14})$$

$$D = \frac{M_o(1 - E1)}{(1 - E1 \cos \alpha)(1 - E2 \cos \beta) - E2(E1 - \cos \alpha)(E2 - \cos \beta)} \quad (\text{B.15})$$

This set of equations represent the behavior of the magnetization before and after the application of an RF pulse when the system has approached steady-state.

The steady-state magnetization in the transverse plane can be written in terms of its components as [89]

$$\vec{M}_{xy}(t) = M_y(t) + jM_x(t) \quad (\text{B.17})$$

in which case $\vec{M}_{xy}^+$ can be rewritten as

$$\vec{M}_{xy}^+ = D \sin \alpha [1 - E2e^{-j\beta}] \quad (\text{B.18})$$

To calculate the evolution of the magnetization vector between RF pulses during the steady-state regime, Equations B.9 to B.11 can be introduced into Equations A.8 yielding

$$M_x(t) = D \sin \alpha [E2 \sin[\beta - \beta(t)] + \sin \beta(t)] E2(t) \quad (\text{B.19})$$

$$M_y(t) = -D \sin \alpha [E2 \cos[\beta - \beta(t)] + \cos \beta(t)] E2(t) \quad (\text{B.20})$$

$$M_z(t) = D[E2(E2 - \cos \beta) + (1 - E2 \cos \beta) \cos \alpha] E1(t) + M_o(1 - E1(t)) \quad (\text{B.21})$$

which translated following Equation B.17 leads to

$$\vec{M}_{xy}(t) = D \sin \alpha E 2(t) e^{j\beta(t)} [1 - E 2 e^{-j\beta}] \quad (\text{B.22})$$

$$= E 2(t) e^{j\beta(t)} \vec{M}_{xy}^+ \quad (\text{B.23})$$

for $0 < t < TR$

Optimum Flip Angle

The SFP equations indicate that the components M_x^+ and M_x^- have the same dependence on the flip angle α . By varying α it is possible to obtain the optimum signal for a predefined value of β . The computation of the optimum flip angle, α_{opt} , involves the maximization of the signal that contributes to the formation of the transverse magnetization M_{xy}^+ with respect to α . This occurs when

$$\cos \alpha_{opt} = \frac{E 1 + E 2(\cos \beta - E 2)/(1 - E 2 \cos \beta)}{1 + E 1 E 2(\cos \beta - E 2)/(1 - E 2 \cos \beta)} \quad (\text{B.24})$$

which displays the complicated dependence on β .

Appendix C

Approach to Equilibrium for SSC Sequences

C.0.3 Mechanisms of Signal Formation

The approach to equilibrium for SSC sequences is not as easily visualized as in the case of SSI sequences since the transverse magnetization prior to each RF excitation plays a major role in the signal formation. The application of RF pulses with flip angles different from 180° causes a repeated mixing of the transverse and longitudinal components of the magnetization when the RF interpulse interval is very short.

The mixing of transverse and longitudinal magnetization components is better understood if each RF is considered to separate the transverse magnetization into three components [89], one of them proportional to the longitudinal magnetization that has recovered in the interpulse interval and the other two proportional to the transverse magnetization and its complex conjugate prior to the RF. At the RF, a portion of M_{xy}^- weighted by $\cos^2 \frac{\alpha}{2}$ does not change its phase and continues dephasing till it hits the next RF pulse; the remaining portion of M_{xy}^- , weighted by $\sin^2 \frac{\alpha}{2}$ will reverse its phase and after being rotated by the next RF will refocus at the subsequent RF pulse producing a primary echo.

The longitudinal magnetization has also components proportional to M_{xy}^- and its conjugate. The RF pulse stores these components along the z axis, and after the next RF excites the system, the stored M_{xy}^{*-} will experience a phase reversal to form a

stimulated echo. The term M_{xy}^- after a subsequent pulse behaves as if its previous in phase condition were moved forward in time by a reversal equal to the repeat time, and after being excited again by another pulse, generates a virtual stimulated echo.

The process is repeated for all the RF pulses exciting the system till an equilibrium condition is reached. Another approach has been considered [36] treating this building structure as a geometric series. The generated echo trains, comprised of primary, stimulated and virtual echoes regain coherence at each RF excitation and contribute to the formation of the signal. The condition for an echo formation is that the phase of the precessing isochromats become equal to one another at a particular instant. This occurs when the total accumulated precession angle is zero or modulo 2π so that the phase coherence is restored. Each RF is treated as a combination of three basic pulses: a 0° , a 90° and a 180° , acting on the available magnetization, $\vec{M}^-$, at the time of the RF. This can be expressed as

$$P_\alpha(\vec{M}^-) = \cos^2 \frac{\alpha}{2} P_0(\vec{M}^-) + \sin^2 \frac{\alpha}{2} P_{180}(\vec{M}^-) + i \sin \alpha P_{90}(\vec{M}^-) \quad (\text{C.1})$$

where P_i expresses the transformation that the RF pulse i produces on $\vec{M}^-$. P_0 maintains the phase of part of $\vec{M}^-$ so this portion continues to dephase through the next interval, P_{90} does not change the phase but stores part of $\vec{M}^-$ in the longitudinal plane, and finally, P_{180} reverses the phase of another portion of $\vec{M}^-$. The successive RF pulses generate a complicated tree like structure where an echo occurs when the zero or 2π condition is met.

C.0.4 Characteristics of the SSC approach

The approach to equilibrium for SSC sequences, contrary to SSI sequences, is oscillatory for all flip angles. This oscillatory behavior is demonstrated in Figures C.1a,b, showing the approach to equilibrium for ROAST with flip angles of 5° and 20° , respectively. The number of RF excitations needed to approach steady state for ROAST is independent

of the flip angles utilized and similarly to FLASH, tissues presenting long T_1 and T_2 values will take a larger number of RF excitations to reach steady state.

The oscillatory frequency shown in Figures C.1a,b is strictly dependent on the excitation flip angle applied. For small flip angles (see Figure C.1a), the approach to equilibrium presents a slow variation of the signal, opposite to what is encountered for larger flip angles, for which the oscillatory frequency increases. In the limit of very low flip angles, the behavior of ROAST is similar to that of FLASH.

Figure C.1: Approach to equilibrium for cerebrospinal fluid (CSF), fat, muscle and blood for a ROAST sequence with $TR=8$ ms and a flip angle of 5° (a) and 20° (b), respectively.

Appendix D

Phase Contribution in the Presence of Trapezoidal Gradients Pulses

The phase contribution to the NMR signal is calculated by using the expressions in Equation 5.2. The gradient pulses applied in practice have finite rise and fall times usually driven by ramps or sinusoidal profiles. For the former case, the gradient waveform is trapezoidal.

Table D.1 demonstrates the phase contribution of each portion of a trapezoidal pulse while Table D.2 shows the phase contribution of the three basic building blocks commonly found in gradient waveforms utilized in the imaging sequence. The phase contribution due to stationary, constant velocity and constant acceleration moving spins have been denoted as Φ_s , Φ_v and Φ_a , respectively, and has been calculated only along the x axis. The phase contributions for motion along y and z behave similarly.

$$\begin{aligned}\Phi_s &= \frac{\gamma G_x x}{2} t_r \\ \Phi_v &= \frac{\gamma G_x v_x}{6} (3t_1 t_r + 2t_r^2) \\ \Phi_a &= \frac{\gamma G_x a_x}{24} (6t_1^2 t_r + 8t_1 t_r^2 + 3t_r^3)\end{aligned}$$

$$\begin{aligned}\Phi_s &= \gamma G_x x (t_2 - t_1) \\ \Phi_v &= \frac{\gamma G_x v_x}{2} (t_2^2 - t_1^2) \\ \Phi_a &= \frac{\gamma G_x a_x}{6} (t_2^3 - t_1^3)\end{aligned}$$

$$\begin{aligned}\Phi_s &= \frac{\gamma G_x x}{2} t_f \\ \Phi_v &= \frac{\gamma G_x v_x}{6} (3t_2 t_f + t_f^2) \\ \Phi_a &= \frac{\gamma G_x a_x}{24} (6t_2^2 t_f + 4t_2 t_f^2 + t_f^3)\end{aligned}$$

Table D.1: Phase contribution of ramp up, plateau and ramp down portions of a trapezoidal gradient waveform

$$\Phi_a = \frac{\gamma G_x a_x}{6} [t_2^3 - t_1^3 + \frac{3}{2}(t_2^2 - t_1^2)t_r + (t_2 - t_1)t_r^2]$$

$$\Phi_a = \frac{\gamma G_x a_x}{6} [t_2^3 - t_1^3 - t_1 t_r^2 - \frac{3}{2}t_1^2 t_r - \frac{1}{4}t_r^3]$$

$$\Phi_a = \frac{\gamma G_x a_x}{6} [t_2^3 - t_1^3 + t_2 t_r^2 + \frac{3}{2}t_2^2 t_r + \frac{1}{4}t_r^3]$$

Table D.2: Phase contribution of basic building blocks found in a practical sequence using trapezoidal gradient waveforms.

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