Phase Enhanced Time-of-Flight Magnetic Resonance Angiography

by

Joe P. Grisham

B.S., Aerospace Engineering
University of Southern California 1982

B.A., Psychology
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M.S., Mechanical Engineering
Rice University 1992

Submitted to the Department of Aeronautics and Astronautics in Partial Fulfillment of the Requirements for the Degree of

Master of Science in Aeronautics and Astronautics

at the

Massachusetts Institute of Technology

May 1995

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Signature of Author

Department of Aeronautics and Astronautics
January 6, 1995

Accepted by

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Department of Aeronautics and Astronautics

January 6, 1995

Certified by:  This thesis was reviewed by an ad-hoc committee appointed by the Dean of the Graduate School. The committee's report is attached.

Accepted by:  Professor Harold Y. Wachman
Chairman, Departmental Graduate Committee
To: Dean Perkins
From: D. Cory, A. Koretsky, and G. Brownell
Date: April 11, 1995
Re: review of Joe Grisham’s Masters thesis

Dear Dean Perkins,

We have reviewed the thesis Joe Grisham submitted for a Master’s degree, “Phase Enhanced Time-of-Flight Magnetic Resonance Angiography,” and find it to be an acceptable thesis when judged by the state of the art in 1989. We recommend that the thesis be given a grade of “B.”

Sincerely,

David G. Cory
Assistant Professor of Nuclear Engineering

Alan Koretsky
Associate Professor, Department of Biological Sciences
Carnegie Mellon University

Gordon Brownell
Professor of Nuclear Engineering
PHASE ENHANCED TIME-OF-FLIGHT
MAGNETIC RESONANCE ANGIOGRAPHY

by

JOE P. GRISHAM

Submitted to the Department of Aeronautics and Astronautics on January 9, 1995 in partial fulfillment of the requirements for the Degree of Master of Science in Aeronautics and Astronautics

ABSTRACT

Current procedures in magnetic resonance angiography emphasize either magnitude or phase to isolate blood flow from surrounding tissue. Magnitude imaging of blood flow is intermittent, leading to potential misdiagnosis of stenosis and occlusions. Present phase techniques rely on extensive hardware instrumentation and eliminate the tissue discrimination necessary for accurate identification of structure in the final image.

Spin echo (SE) and gradient echo (GE) protocols were established from theoretical calculations of laminar flow profiles in major vessels of the human abdomen, perineum and upper leg with maximum velocities of 20-90 cm/sec. Sequence parameters for SE acquisition of TR= 100 msec and TE= 20 msec were analytically determined to provide a time-of-flight increase in normalized blood flow signal magnitude of 0.45-0.61, above the stationary body fat (0.36) and muscle (0.12) levels. GE parameters of TR= 20 msec, TE= 11 msec and theta= 40° predicted an increased signal magnitude of 0.30-0.55, compared to stationary fat and muscle tissue values of 0.23 and 0.09 respectively. Phase was defined as a linear function of velocity.

Experimental results agreed with the analytical GE protocol mapping the increased signal to white in intermediate magnitude image gray scale for arterial and venous flow through transverse MRI sections. The SE protocol produced white blood in venous flow but diminished in gray scale value for high velocity arterial flow. Venous flow was defined by mid-level gray scale in the corresponding intermediate phase image for the same MRI acquisition. Increased velocity in the major arteries mapped intraluminal phase toward black. Enhancing the intermediate magnitude image by computer graphic addition of inverted phase generated a complete angiogram presenting blood flow as highest intensity within the slice and retaining gray scale definition of body tissues.
BIOGRAPHICAL NOTE

JOE P. GRISHAM

Joe Grisham was born in the small East Texas industrial town of Lufkin on November 27, 1950. His father was a plant electrician and his mother, County Clerk. Early years were spent in the fundamental study of piano, mathematics and architecture.

He entered the university at Texas A&M in Architecture Design; but, after one year, at the accidental death of his fiancée's father, he returned to East Texas and married his wife, of now twenty-four years. In the immediate years following, they had one daughter and one son. He continued part time studies in mathematics, philosophy and psychology as he worked in the trades as a carpenter, machinist and structural lay-out of oil field pumping units.

Grisham enlisted in the US Air Force in 1975 as an avionics navigation specialist. Following completion as Honor Graduate from both Basic Training and Avionics Technical Schools, he worked flight-line maintenance of F-4 and F-105 Tactical Air Command aircraft returning from Thailand. In three years active duty his technical experience increased from navigation to communication, instrumentation and weapons control. In 1978 he competed for the Airman Education and Commissioning Program, and, on acceptance, was assigned full-time to the University of Southern California.

He entered a dual-degree program for the BS Aerospace Engineering and BA in Experimental Psychology. There he began detailed engineering applications to physiological questions. He spent several semesters in research labs developing the hardware data acquisition, coding software analysis and performing the stereotactic surgery to implant bipolar electrodes in the brains of mice for research of Parkinson's disease.

Following completion of the BS/BA degrees at USC and commissioning as 2Lt from Officers Training School, he began an assignment as Flight Stability and Control Engineer at Wright Patterson AFB, Ohio. Over the next five years he developed the analytical evaluation of aircraft design with respect to human tolerance to vibration, wrote the stability and control appraisal to acquire the F-15E and approved first-flight stability and control of the AFTI F-111 experimental variable camber Mission Adaptive Wing. But his most decorated accomplishment came in the Air Force Achievement Medal for design and development of the Mishap Investigation facility where he combined computer graphic modeling with flight stability and control derivative simulations and defense mapping data of actual terrain to recreate mishap scenarios for Investigation Boards.

During this tour Grisham began advanced studies in human anatomy, physiology and information processing in the nervous system. He was accepted to the Graduate School at Wright State University in the Department of Anatomy and spent many off-duty hours in special dissections particularly
in describing gross variations circulation with tumor growth. In 1987, at the end of the active duty tour, he left Wright Patterson to take up graduate work at the Massachusetts Institute of Technology with inter-institutional study at Harvard Medical School.

The first month in Boston his wife was in an auto accident that completely severed two fingers. Grisham became affiliated with the Massachusetts General Hospital as a volunteer with the Plastic Surgery team that successfully reattached his wife's fingers. He later promoted to on-staff as Research Associate with the Department of Radiology where he published his first works-in-progress paper, *MR Angiography of Pelvic Blood Vessels by Coronal Reconstruction*, in Magnetic Resonance Imaging. The following issue of Diagnostic Imaging showcased the presentation of the paper as a highlight of the SMRI Conference.

He completed the Master of Science degree at Rice University in 1992. The thesis designed and implemented a low voltage fingertip force feedback control system for a three-fingered dexterous robotic hand. He continued anatomy research at Baylor College of Medicine where he lectured on normal gross structure and variations following amputation. The robotic thesis work was extended to prosthetic hand control for children with congenital forearm defects and, presented to the US House Appropriations Committee meeting on the transfer of technology to medicine.

Grisham presently lives in Fort Worth with his wife, an LVN in cardiac telemetry. He remains a Captain in the Air Force Reserve with an occupation as Medical Research engineer, currently evaluating surgical procedures and interactive forces on instruments during laparoscopic operations.
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1 INTRODUCTION

1.1 Development of Magnetic Resonance Angiography

Decades before clinical magnetic resonance imaging (MRI), nuclear magnetic resonance (NMR) relaxation time was used to qualify blood flow. Even then, NMR techniques were proposed for non-invasive human angiography over the traditional injection of radiopaque tracers. Despite this apparent long history, no universal clinical MRI angiographic protocols have been established. The current ability to image vascular blood flow is divided between an emphasis on either (1) time-of-flight magnitude enhancement or (2) phase shift.

In 1959, Singer proposed NMR for tracing the flow of specific materials in the body and demonstrated adiabatic fast passage of blood flow in mice tails [1]. Eleven years later, Morse and Singer, with hardware improvements, used similar NMR methods with a tagged bolus to measure blood velocity in the median vein of the human forearm [2].

The follow-on development of MRI led to several unique observations of flow, predominately in transverse slices through the human abdominal aorta and inferior vena cava. Initially seen as "paradoxical enhancement" and "phase artifact", the bright and dark areas in images of vessel lumen later became understood as nonlinear affects of flow in MRI dependent on sequence protocol, blood vessel geometry and flow velocity.

Figures 1.1, 1.2 and 1.3 illustrate the affects of blood flow on image intensity. All images represent a 1 cm thick transverse MRI slice taken along the x,y plane in Figure 1.6A. A Gradient Echo (GRE) protocol of Figure 1.1
generates the classical "paradoxical enhancement" of white blood flow through both the aorta (a) and inferior vena cava (ivc).

Figure 1.1

Axial Gradient Echo MRI with "Paradoxical Enhancement"

(Protocol: General Electric mode Multi GRE/60; TR= 33; TE= 15)

A Multi Echo (ME) sequence of the same slice (Figure 1.2) produces a flow void (black) in both vessels. The decrease in sequence repetition time (TR) combines with velocity profiles and multiple slice acquisition to generate a variety of bright and dark signal intensities across the ivc and aortic lumen of Figure 1.3.
Figure 1.2
Axial Multi-Echo MRI with Dark Blood Flow
(Protocol: General Electric Multi ME mode; 1 echo; TR= 1000; TE= 25)

Figure 1.3
Axial Multi-Echo MRI with Variable Intensity Flow
(Protocol: General Electric Multi ME mode; 1 echo; TR= 300; TE= 25)
The principle blood flow effects on MRI have been explained in three processes: (1) washout of excited spins from the slice being imaged, (2) washout of saturated spins from the slice being imaged with replacement by unsaturated spins from upstream, and (3) motion along the magnetic field gradients resulting in phase shifts accompanied by a decrease in signal [3].

The first two processes are generally combined into time-of-flight effects. The third category is termed phase-shift effects.

1.2 Time of Flight versus Phase Shift

The basic principles of time-of-flight are straightforward. The time interval between excitation and reading the magnetic resonance signal provides a window where velocity can affect the measured signal amplitude. Excited proton spins leaving the slice (washout) before being read decrease total signal from the sample. Residual saturation of spins (either remaining in the slice or coming in from multi-slice techniques) reduces the signal produced by subsequent excitation pulses. Conversely, wash-in of fully relaxed spins between excitation pulses has the potential to increase signal. Image scan parameters are generally tailored to take advantage of wash-in and wash-out effects in visualizing flow.

The second component of flow related effects is phase shift. When processing proton spins move along a magnetic field gradient, they exhibit a frequency shift related to their velocity in the gradient direction [4]. This observation has been developed into an MRI angiographic sequence to image vessels carrying pulsatile flow using mean velocity dependent phase contrast, electrocardiac gating and image subtraction of concurrent acquisitions [5, 6].
Phase sensitive angiography has also been demonstrated to visualize slower venous flow [7] and expanded with 3-dimensional gradient modulation to generate projection angiograms of peripheral arteries and veins [8].

Although phase angiography has been presented as more accurate than time-of-flight in qualifying flow, it depends on subtraction techniques to visually isolate vessels. The surrounding stationary tissues and their respective landmarks are absent in the final image as shown in Figure 1.4.

Figure 1.4

Image from Cardiac Gated Phase Contrast Subtraction
(Ref. [5] Figure 3, Superficial Femoral (sfa) and Deep Femoral Arteries (dfa))

Time of flight methods and phase shift effects are not completely independent. Magnitude enhancement protocols can generate substantial phase artifacts from flow moving through the slice in 2-dimensional Fourier transform (2DFT) images. These artifacts appear as spatial misrepresentations in the phase encode direction as seen in the ghost images above and below.
the aorta of Figure 1.1. Bilateral saturation (SAT) protocols are often used to suppress flow motion phase artifacts. The saturated nuclei (blood flow) moving into an image slice give no signal with successive excitations. Phase artifacts are removed; but, all flow information is lost.

1.3 MRI Angiography Display: Image Reconstruction

Information about flow in a particular vessel appears in both magnitude and phase of the composite magnetic resonance signal. There are several mathematical processes to display that information; and, each process is inherently as important as the MRI protocol to acquire the signal. Back projection and 2DFT are the mathematical processes most rigorously expanded in texts; 2DFT and Intermediate Images are more common to the clinical setting.

While 2DFT is predominate, most clinical MRI systems have the option to create several intermediate images for display or calculation of other images [9]. Intermediate image reconstruction for spin echo protocol is illustrated in Figure 1.5. The sampled composite signal is compared to a radio-frequency (RF) reference near the magnetic resonant frequency and demodulated into two components. The Real component is that part of the composite signal directly in phase with the reference signal. That part 90 degrees out of phase with the reference makes up the Imaginary component of the signal.
Figure 1.5
Intermediate Image Construction and Display
(Ref. [9] Figure 2-13 A, B, C)
Real and Imaginary components can each be converted by Fourier Transform into a 2-dimensional image. If there is no phase shift, then the Real image represents the true magnetization vector of the sample. If there is a phase shift, the Real image only represents a portion of the magnetic resonance signal while a component of the signal appears in the Imaginary image. Even though the Real image can be displayed in Inversion Recovery (IR) MRI sequences, a Modulus (or Magnitude) display is generally computed from Real and Imaginary terms. This Magnitude reconstruction eliminates phase errors in motion and magnetic field inhomogeneities but sacrifices phase information of blood flow. Flow information is maintained in the Phase display calculated from Real and Imaginary images of the same MRI scan.

In addition to clinical operator displays, off-line computer graphics (Figure 1.6) is vastly increasing the range of available digital image processes for clinical diagnosis. 2-dimensional gradient and threshold algorithms commonly provide tools to outline and interpret structures in MRI images. Single slice acquisitions reformatted for 3-D ray tracing operations offers a host of viewports and user interactions. The most promising approach may come in tailoring MRI protocols for specific post processing algorithms.
Figure 1.6
Technicare Magnet Coordinate System with Off-line Digital Signal Processing

A: Principle planes of the Technicare MRI coordinate system [Ref. 10, Figure 8].
B: Clinical Display with Off-line Digital Image Processing
1.4 Thesis Outline

The effect of velocity on MRI signal intensity provides a basis for non-invasive angiography. Most techniques, however, require specialized pulse sequences not generally used for routine clinical imaging [11]. Others are limited to cardiac gating and time prohibitive for patient imaging. The following thesis derives clinical MRI sequences that take advantage of human flow velocity profiles for the display of major blood vessels in the human abdomen, perineum and upper leg. Protocol minimize imaging time and require no cardiac gating.

Initial emphasis is placed on calculating the maximum enhancement from time-of-flight effects in the Modulus image. That is, increasing the magnitude vector of flow. Given the phase information that is available in the same clinical MRI acquisition, subsequent chapters introduce a digital post processing combination of phase and magnitude images to improve the final presentation over that produced by magnitude considerations alone.

Chapter 2 provides an overview of human angiology in major vessels of the abdomen, perineum and upper leg. The anatomical structure and intraluminal dimensions determine which vessels will be visible in transverse MRI scans. Fundamental engineering fluid dynamic principles are used to evaluate velocity profiles of blood flow in the normal physiologic vessels of the region. Angiology and fluid dynamic principles applied to determine the numerical values required of MRI scan parameters in later chapters.

Chapter 3 describes the theoretical image contrast enhancement from laminar flow through an MRI cross-section of a rigid tube. These mathematical predictions are extrapolated in Chapter 4 to calculate
experimental sequence parameters to enhance signal intensity from blood flow in the major vessels of the region over that of fat and muscle tissue. Experimental MRI parameters are presented to maximize blood flow signal intensity in gradient echo and spin echo images at minimum patient scan time.

The actual experiments are described in Chapter 5. Results and Discussion are presented in Chapters 6 and 7.

Appendix A provides the derivation of average flow from axial flow velocity. Appendices B and C define the Basic computer programs and tabulate numerical results for theoretical time-of-flight signal intensity under varied parameters for spin echo and gradient echo MRI sequences. Appendix D details the C programs used in digital image post-processing.
Magnetic resonance angiography in single slice acquisition is strictly dependent on the size, orientation and intraluminal flow of the vessels being observed. The intraluminal size determines which vessels will be visible under the spatial resolution of the system. Orientation of the vessel with respect to the acquisition slice and the type of flow within that vessel define the maximum contrast resolution of blood flow in the final image.

A complete description of the major arteries and veins is appropriate for analyses and interpretation of these parameters. The following chapter illustrates the major blood vessels in the abdomen, perineum and upper regions of the leg, first in terms of structural anatomy, then with respect to intraluminal flow velocity. Anatomy and velocity profiles are combined in the final aspect of this chapter to generate numerical values required to determine the experimental maximum flow contrast MRI protocols.

2.1 Angiology

The major blood vessels in the region of interest are illustrated in Figures 2.1 and 2.2. Figure 2.1 is an MRI coronal section (x,z plane of Figure 1.6) at the aortic bifurcation of the experimental subject (Chapter 5). Figure 2.2 provides an artistic definition of the arteries and veins described in the following sections.
Figure 2.1
MRI Coronal Section

Figure 2.2
Major Abdominal Vessels
(in part from Ref. 24, Fig. 261)
2.1.1 The Arterial System

The abdominal aorta begins at the aortic hiatus of the diaphragm and descends in the median plane just anterior to the vertebral column. It ends slightly to the left of midline by dividing into the left and right common iliac arteries. The superior abdominal aorta is separated from the inferior vena cava by the right crus of the diaphragm. The distal abdominal aorta is in direct contact with the inferior vena cava below the level of the second lumbar vertebra and, to some extent, overlays the left psoas major muscle.

The first relation of the abdominal aorta is the coeliac trunk which branches predominantly trans-axial. Immediately below the coeliac trunk, the superior mesenteric artery descends in front of the left renal vein behind the body of the pancreas. Below the level of the superior mesenteric artery, right and left renal arteries extend laterally at approximately right angles.

The abdominal aorta divides on the left side of the fourth lumbar vertebra into right and left common iliac arteries. Bifurcation is symmetrical at a mean angle of 37 degrees [12]. The right common iliac artery is separated from the bodies of the fourth and fifth lumbar vertebra by the inferior vena cava. Laterally, it is adjacent to the inferior vena cava, right common iliac vein and psoas major. Medial, the upper portion of the right common iliac artery is adjacent to the left common iliac vein. In front, both left and right common iliac arteries are crossed by the ureter and covered by peritoneum which separate them from the coils of small intestine. The left common iliac artery is shorter than the right. The left common iliac vein lies between the artery and the bodies of the fourth and fifth lumbar vertebrae. Laterally, the artery is bordered by left psoas major muscle.
Common iliac arteries bifurcate at the level of the sacroiliac joint into two branches **external and internal iliac arteries.** The internal iliac artery supplies the viscera, walls of the pelvic, perineum and gluteal regions. The external iliac artery descends to supply the greater part of the lower limb. Each external iliac artery runs along the respective medial border of psoas major from the bifurcation of the common iliac artery to the anterior superior iliac spine. There it enters the leg behind the inguinal ligament to become the **femoral artery.**

The femoral artery is the principle artery of the lower limb. It travels in the lateral compartment of the femoral sheath, passing in the femoral triangle along the front and medial aspect of the thigh. At the base of the femoral triangle, the artery is separated from the capsule of the hip joint by the tendon of psoas major. More distally, it is separated from pectineus and adductor longus muscles by the **femoral vein.** At the apex of the femoral triangle, the artery enters the adductor canal where it lies behind sartorius and in front of adductor longus muscles and is bordered anterolaterally by vastas medialis muscle.

The **arteria profunda femoris** branches from the lateral side of the femoral artery below the inguinal ligament. It then passes behind the femoral artery and femoral vein on the medial side of the femur where it lies between pectineus and adductor longus muscle.

### 2.1.2 The Venous System

In general, veins of the abdomen, perineum and lower limb accompany the corresponding artery as described in the previous section. The
exceptions are the superficial saphenous veins of the leg and hepatic portal system of the liver.

The great saphenous vein begins in the medial marginal vein of the foot and ends in the femoral vein below the inguinal ligament. It runs upwards along the medial side of the thigh and passes through the saphenous opening below and lateral to the pubic tubercle. A fairly constant large vessel, sometimes called the anterior femoral cutaneous vein, commences from a network of veins on the lower part of the front of the thigh and crosses the apex of the femoral triangle to enter the great saphenous vein.

The hepatic portal vein conveys blood to the liver from the abdominal part of the digestive track, spleen, pancreas and gall bladder.. From the liver, blood enters the inferior vena cava by way of the hepatic veins.

2.2 Fluid Mechanics in Blood Flow

2.2.1 Reynolds' Number

Fluid mechanics defines three general types of flow in cylindrical tubes: inviscid, laminar and turbulent (Figure 2.3). Inviscid flow is characterized by an almost flat plug like velocity distribution over the radius of the tube. Mathematically, this type of flow is described by $\frac{du}{dy} \equiv 0$. In Laminar flow, $\frac{du}{dy}$ or $\frac{dv}{dy}$ does not equal zero (where $u= \frac{dx}{dt}$, $v= \frac{dy}{dt}$); instead, the velocity profiles are smooth curves with fluid particles following fixed streamlines. Turbulent flow is characterized by random fluctuations in fluid velocity and a mixing of streamlines.
Inviscid flow is very much a theoretical concept that involves frictionless fluid. It has application only where velocity changes are very small over a short distance perpendicular to the velocity vector and where the fluid has very low viscosity. Blood, by contrast, is a viscous suspension of particles and open to flow analysis by Reynolds' number (Re), defined in equation 2.1. The dimensionless Re is directly proportional to the radius (r) of the cylindrical vessel and the mean velocity (V_{avg}), and inversely proportional to the kinematic viscosity (\mu = \eta/\rho):

\[
Re = \frac{V_{avg} \cdot 2r}{\mu} \tag{2.1}
\]

Reynolds' number suggests whether the flow is laminar or turbulent. Engineering experimental evidence indicates if Re number is "small", the flow will be laminar; if "large", the flow is turbulent. Engineering Re numbers below 1000 are generally considered small, and, those above 1000, large [13]. In theory, viscous fluids would have laminar flow until they reached the critical Re number of 1000 then transition to turbulent flow. In
practice, the precise definition of a critical Re number must be determined by experiment for both increasing and decreasing velocities.

Applying these concepts to blood flowing through rigid tubes of 0.126 to 0.34 cm in radius, the critical Re number for blood has been experimentally determined at 2000; and, from limited data available in humans, Re numbers are well below 2000 throughout the circulation except at the root of the aorta and in the pulmonary arteries, where values of 5,000 to 12,000 are reached during systole [14]. So, under normal physiological conditions, flow is laminar in the regional vasculature of the abdomen, perineum and upper thigh [15].

2.2.2 Poiseuille's Law

Poiseuille's law (equation 2.2) governs laminar flow in cylindrical tubes. The flow rate $Q$ is calculated as:

$$Q = \frac{(P_1 - P_2) \pi r^4}{8\mu L} \tag{2.2}$$

$P_1$ and $P_2$ are the respective pressures at either end of a cylinder of length $L$ and radius $r$ with fluid of kinematic viscosity $\mu$. The physical and mathematical boundary conditions under which this law applies are:

1. Fluid is homogeneous and its viscosity is the same at all rates of shear.
2. The rate of flow is steady not subject to acceleration or deceleration.
3. Flow is laminar, all points moving parallel to the wall.
4. The liquid does not slip at the wall, an assumption required for the constant of integration.
5. The tube is long compared to the region being studied.
and

(6) The tube is rigid so that the diameter does not change in time or distance.

There are several observations that should be noted before analyzing flow in arteries and veins. Poiseuille's law describes constant flow of Newtonian fluids through a rigid pipe, and its application to blood flow in human circulation depends on the extent to which the vascular system conforms to those theoretical conditions. First of all, blood vessels are not rigid cylindrical tubes. They are elastic, constantly under tension and changing in diameter. Second, flow is laminar as a rule but pulsatile rather than constant in most of arterial circulation. Pulsatility is also demonstrated in the larger veins. For example, the normal flow pattern of the vena cava is characterized by 2 or 3 distinct peaks with velocity ranges at the peaks from 15-35 cm/sec to less than zero [16]. As a final objection, the endothelium may be non-wettable[17]. Velocity must go to zero at the wall for equation 2.2 to be valid in this simplified form.

Despite the differences between blood vessels and rigid tubes, Poiseuille's law and Reynolds' number can be used under limited regions of interest: large vessels, normal physiology and laminar flow. With laminar blood flow established by Reynolds' number in the vessels of interest (Section 2.2.1), Piousuille's law is used (Appendix A) to relate maximum velocity ($V_{\text{max}}$) to average blood velocity ($V_{\text{avg}}$) by the equation:

$$V_{\text{avg}} = 0.5 V_{\text{max}} \quad 2.3$$

Section 2.3 establishes the fractional volumes of new blood entering an MRI acquisition slice using $V_{\text{max}}$ as the vertex of a paraboloid. Section 2.4 uses
equation 2.3 to define \( V_{\text{avg}} \) or \( V_{\text{max}} \) when one is not available in the literature. Chapter 3 applies the fluid mechanic principles of maximum velocity over parabolic laminar flow profiles to calculate the amount of specific segment contribution to magnetic resonance signal intensity.

### 2.3 Fractional Volume in Blood Vessels

The cylindrical volume cut by an acquisition slice is \( \pi d^2 L / 4 \) where \( d \) is the vessel diameter and \( L \) is the slice thickness.

![Figure 2.4](image)

For laminar flow through a vessel, the Fraction Volume \( (F_n) \) of new blood entering the slice is computed as a paraboloid of revolution \( \{(1/2) \pi d^2 V_{\text{max}} / 4\} \) normalized by the volume of the cylinder. There are several variations of \( F_n \) depending on the boundary conditions:

1. If \( V_{\text{max}} T \leq L \) the parabolic volume stays totally within the slice (Figure 2.5) and the Fractional Volumes within the cylinder are:
Figure 2.5
Boundary Condition: $V_{\text{max}}T \leq L$

\[ F_a = \frac{V_{\text{max}}T}{2L} \]
\[ F_b = 1 - F_1 = 1 - \left(\frac{V_{\text{max}}T}{2L}\right) \]

2. If $V_{\text{max}}T > L$ part of the volume passes outside the slice:

Figure 2.6
Boundary Condition: $V_{\text{max}}T > L$

Integrating the parabola as a solid of revolution with upper limit $V_{\text{max}}T$ and lower limit $(V_{\text{max}}T) - L$ gives:

\[ F_c = 1 - \left(\frac{L}{2V_{\text{max}}T}\right) \]
\[ F_d = 1 - F_3 = \frac{L}{2V_{\text{max}}T} \]
2.4 Thesis Representation: Expectations and How the Anatomy and Blood Flow Will be Modeled

Certainly what we expect to observe depends on the spatial resolution of our image. In this particular study, instrumentation spatial resolution is 45 cm/256 pixels, or 0.176 cm/pixel. Vessels, with lumen this size and smaller, contribute only part of the pixel intensity in the final image. Lumen diameters of the major blood vessels in the abdomen perineum and upper leg (see Figure 2.8) range from 2.20 cm (aorta) to 0.68 cm (profunda femoris). The relationship between MRI pixel and lumen size is illustrated in Figure 2.7.

![Diagram of Aorta and Profunda Femoris Lumen](image)

Aorta Lumen
2.20 cm D (12.50 pixels)

Profunda Femoris Lumen
0.68 cm D (3.86 pixels)

Figure 2.7
Relative Size of MRI Pixels over the Range of Vessel Lumen

Orientation of the flow axis also limits which vessels will be visible in a flow enhanced image. In axial MRI slices, flow through blood vessels running superior-inferior will be enhanced. Vessels traveling predominately medial-lateral or anterior-posterior will not be affected.
In addition to spatial resolution and flow axis orientation, the ability to define vessels in magnitude reconstruction depends on distinguishing blood flow from the surrounding static tissue. This is referred to as contrast resolution. Even though the procedures involved may be generalized to time-of-flight and phase techniques, the expected contrast resolution is unique to the particular MRI protocol executed. Contrast using the velocity contribution to enhance flow is the topic of Chapter 3.

Thesis specifications for the structural anatomy and blood flow velocity distributions in the vessels of the abdomen, perineum and upper leg are defined in Figures 2.7 and 2.8. Unless otherwise noted, lumen diameters, cross-sectional area, maximum velocity and average velocity values are stated from anatomical [11] and physiological [12] texts. * denotes the value was calculated from Equation 2.3.
Figure 2.7
Thesis Definition of Anatomy and Flow Velocity in Major Arteries of the Abdomen, Perineum and Upper Leg
Inferior Vena Cava
Lumen
diameter: 1.4 cm
cross-sectional area: 1.5 cm²
Flow Velocity
maximum: 20.3 cm/sec
average: 20.0 cm/sec

Hepatic Portal Vein
Lumen
diameter: 1.00 cm
cross-sectional area: 0.80 cm²
Flow Velocity
maximum: 20.0 cm/sec
average: 17.0 cm/sec

Common Iliac Vein
Lumen
diameter: 1.63 cm
cross-sectional area: 2.09 cm²
Flow Velocity
maximum: 30.0 cm/sec*
average: 15.0 cm/sec

Internal Iliac Vein
Lumen
diameter: 1.15 cm
cross-sectional area: 1.04 cm²
Flow Velocity
maximum: 30.0 cm/sec*
average: 15.0 cm/sec

External Iliac Vein
Lumen
diameter: 1.15 cm
cross-sectional area: 1.04 cm²
Flow Velocity
maximum: 30.0 cm/sec*
average: 15.0 cm/sec

Femoral Vein
Lumen
diameter: 0.98 cm
cross-sectional area: 0.74 cm²
Flow Velocity
maximum: 30.0 cm/sec*
average: 15.0 cm/sec

Saphenous Vein
Lumen
diameter: 0.98 cm
cross-sectional area: 0.74 cm²
Flow Velocity
maximum: 20.0 cm/sec*
average: 10.0 cm/sec

Figure 2.8

Thesis Definition of Anatomy and Flow Velocity
in Major Veins of the Abdomen, Perineum and Upper Leg
The signal observed in proton MRI measures the magnetization vector in the transverse (x,y) plane. Signal intensity is then proportional to the amount of magnetization vector rotated into the transverse plane and the time it remains there. Figure 3.1 illustrates the vector magnitude and phase polar coordinate representation.

![Diagram of magnetization vector in NMR](image)

Figure 3.1  Polar Coordinate Representation
In the context of this thesis:

\[ B_0 = \text{static magnetic field aligned with the z axis of the magnet as shown in Figure 1.6A} \]

\[ B_1 = \text{resonant field in the rotating } (\omega_0) \text{ coordinate frame} \]

\[ \omega_0 = \text{Larmor frequency. } \omega_0 = \gamma B_0, \text{ where } \gamma \text{ is the magnetogyric ratio} \]

(For hydrogen \( \gamma = 42.57 \text{ MHz/Tesla}. \))

\[ M_0 = \text{equilibrium magnetization vector} \]

\[ M = \text{magnetization vector with components } M_x, M_y \text{ and } M_z \text{ in the rotating coordinate frame} \]

\[ \phi = \text{phase angle: } \text{atan } (M_y / M_x) \]

\[ x,y = \text{transverse (axial) plane of Figure 1.6A.} \]

\[ z = \text{longitudinal axis of Figure 1.6A} \]

**90° pulse** (\( \pi/2 \text{ pulse} \)) = smallest input radiofrequency (RF) pulse needed to elicit a maximum magnetic resonance signal

**180° pulse** (\( \pi \text{ pulse} \)) = input RF quantity twice that of a \( \pi/2 \text{ pulse} \)

Immediately following a 90° pulse, a component of the longitudinal magnetization \( (M_0) \) lies in the transverse plane \( (x,y) \) and begins to process around the \( B_0 \) axis. The magnetic resonance signal is sinusoidal, oscillating at the Larmor frequency. Ideally the magnetization vector \( (M) \) follows the solution to classical Bloch equations in the rotating \( \omega_0 \) coordinate frame:

\[ M_x(t) = M_x(0) e^{-t/T_2} \quad 3.1 \]

\[ M_y(t) = M_y(0) e^{-t/T_2} \quad 3.2 \]

\[ M_z(0) = M_0 (1 - e^{-t/T_1}) + M_z(0) e^{-t/T_1} \quad 3.3 \]
where \( \mathbf{M}(0) \), \( \mathbf{M}_x(0) \), \( \mathbf{M}_z(0) \) are the components of \( \mathbf{M} \) at time \( t=0 \).

**T1** = time constant (length of time required) for a substance to regain 63% of its equilibrium longitudinal (\( \mathbf{M}_z \)) magnetization. T1 limits the time between TR: generally TR = 5 T1.

**T2** = true time required for sample (tissue) transverse magnetization (\( \mathbf{M}_x, \mathbf{M}_y \)) in a free induction decay to loose 63% of its original value. T2 limits time the signal is available to be read.

Actually, if the magnetic resonance signal is read under Free Induction Decay, the magnitude (\( \mathbf{M}_{x,y} \)) in the transverse plane is dependent on the magnet used:

\[
\begin{align*}
\mathbf{M}_x(t) &= \mathbf{M}_x(0) e^{-t/T_2^*} \\
\mathbf{M}_y(t) &= \mathbf{M}_y(0) e^{-t/T_2^*}
\end{align*}
\]

**T2^*** = time required for transverse magnetization in a free induction decay to reach 37% of its original value. T2^* is a function of the true T2 and inhomogenous fields within the magnet. T2 is used in theoretical calculations of Chapters 3 and 4. T2^* is inherent to the measured signal in the experiment.

Equations 3.1 - 3.5 introduce the fundamental signal magnitude measured in MRI to define MRI parameters as they apply to this thesis. There are many factors that describe the action of the magnetization vectors at the molecular level under a variety of experimental conditions. Details are referred to numerous NMR and MRI texts. Here emphasis is placed on the parameters affecting magnetic resonance signal at the sample (or voxel) level; that is, the parameters in the MRI scan protocol (pulse sequence) that affect
the macroscopic vector (1) magnitude, (2) phase, (3) relaxation away from the transverse (x,y) plane and (4) return to the longitudinal (z) axis. Additional common MRI scan parameters defined in the context of this thesis are:

\[ \text{TR} = \text{repetition time between MRI pulse sequences} \]
\[ \text{TE} = \text{time of MRI spin echo following a rephasing (180 degree) RF pulse} \]
\[ G_x, G_y = \text{magnetic field gradients introduced for spatial encoding in the axial plane} \]
\[ G_z = \text{slice select gradient along longitudinal axis} \]

Each parameter (T1, T2, TE, TR, RF pulse, gradients) can be tailored within a particular MRI scan sequence to enhance a specific quality. An MRI scan sequence is often tailored to exploit image contrast between tissues (i.e., making white matter of the brain bright and gray matter dark). These same parameters may also be tailored to exploit flow as opposed to static tissue. Theoretical predictions to enhance flow through rigid tubes are presented in Section 3.2 and 3.3 for Spin and Gradient Echo MRI sequences. Chapter 4 calculates the actual thesis scan parameters used to enhance the flow imaged through major vessels of the abdomen, perineum and upper leg.

**3.2 Time of Flight Effects in Spin Echo and Gradient Echo MRI**

Two pulse sequences were chosen to image blood flow in the abdomen, perineum and upper thigh: Spin Echo and Gradient Echo. All sequences are single slice acquisition to prevent temporal influences on flowing spins entering the slice selected. Each sequence is explained below.
3.2.1 Spin Echo

The spin echo sequence is diagrammed in Figure 3.2.

Conventional spin echo imaging collects the projection signal from spin echo peak generated by a 90-180° pulse pair. \( G_z \) is the slice select gradient. The 90° pulse generates transverse magnetization \( (M_x,M_y) \) by rotating longitudinal magnetization \( (M_0) \) into the xy plane. The signal is read at time TE in the form of a refocused spin echo induced by the subsequent 180° pulse. Image signal intensity \( (S) \) for the spin echo sequence is given by:
\[ S = M_0 [1 - \exp\left(-\frac{(TR-TE)}{T1}\right)] \exp\left(-\frac{TE}{T2}\right) \] 3.6

In Spin Echo imaging:

**TR** = repetition time between 90° pulses

**TE** = echo time (time between the 90° pulse and spin echo)

In Spin Echo imaging there are two effects on the composite signal from increasing blood flow velocity through the axial slice: (1) Phase changes due to flow along the slice (z) gradient (Section 3.3), and (2) Signal magnitude decreases due to washout of excited spins between the 90° slice select and 180° refocusing pulse.

Gullberg et al [20] show the spin echo fractional signal intensity contribution from each velocity population in laminar flow can be calculated as follows:

(Equations 3.7-3.15 modified from [20] to be consistent with thesis terminology.)

**Velocity Population Profiles for \( V_{\text{max}} \leq L/(TR + TE/2) \)**

**Figure 3.3**
From Figure 3.3:
At the time of the 180° refocusing pulse spins in region 0) entered after the
90° but before the 180° pulse; therefore, they do not possess transverse
magnetization and contribute no signal

\[ S_0 = 0 \]  

3.7

Spins in population a entered in the interval TR - TE/2. They experienced
a 90° and 180° to produce a signal \( S_a \):

\[ S_a = M_o e^{-TE/T_2} \]  

3.8

Population b entered the slice in the interval TE/2 - TR of the
previous cycle, therefore has experienced a 180° pulse followed a time (TR
- TE/2) later by 90° pulse, then TE/2 later by a 180° refocusing pulse. The
signal from population b \( S_b \) is then:

\[ S_b = M_o \{ 1 - 2e^{-[(TR - TE)/2]/T_1} \} e^{-TE/T_2} \]  

3.9

Spin population c consists of all spins entering before the 90° pulse
of the previous cycle and:

\[ S_c = M_o \{ 1 - 2e^{-[(TR - TE)/2]/T_1 + e^{-TR/T_1}} \} e^{-TE/T_2} \]  

3.10

The total signal \( S_{total} \) arising from the slice is the sum of the population
signals weighted by their respective fractional volumes \( (F_a, F_b, F_c) \):

\[ S_{total} = S_a F_a + S_b F_b + S_c F_c \]  

3.11
Increasing velocity effects are shown in Figures 3.4 through 3.6.

Velocity Population Profiles for $\frac{L}{(TR + TE/2)} < V_{\max} \leq \frac{L}{TR}$

Figure 3.4

Velocity Population Profiles for $\frac{L}{TR} < V_{\max} \leq \frac{L}{(TE/2)}$

Figure 3.5

Velocity Population Profiles for $V_{\max} > \frac{L}{(TE/2)}$

Figure 3.6
Note that as the velocity increases the total signal over the vessel lumen is predicted to decrease for single echo: spin echo sequences. Figures 3.3 - 3.6 represent four velocity dependent boundary conditions on Equation 3.11. From the fractional volumes presented in the previous section, Gullberg [20] calculates the total signal ($S_{total}$) across length $L$ of laminar flow in a rigid tube as:

1. IF $V_{max} \leq L/(TR + TE/2)$
   \[
   S_{total} = S_a \left[ V_{max} (TR - TE/2)/(2L) \right] + S_b V_{max} TE/(4L) + S_c \left[ 1 - V_{max} (TR + TE/2)/(2L) \right] \tag{3.12}
   \]

2. IF $L/(TR + TE/2) < V_{max} \leq L/TR$
   \[
   S_{total} = S_a \left[ V_{max} (TR - TE/2)/(2L) \right] + S_b \left[ 1 - L/[2V_{max}(TR + TE/2)] - V_{max}(TR/2L) \right] + S_c L/[2V_{max} (TR + TE/2)] \tag{3.13}
   \]

3. IF $L/TR < V_{max} \leq L/(TE/2)$
   \[
   S_{total} = S_a \left[ 1 - L/(2V_{max}TR) - V_{max}TE/(4L) \right] + S_b \left[ L/(2V_{max}TR) - L/[2V_{max}(TR + TE/2)] \right] + S_c L/[2V_{max} (TR + TE/2)] \tag{3.14}
   \]

4. IF $V_{max} > L/(TE/2)$
   \[
   S_{total} = S_a \left[ L/(V_{max}TE) - L/(2V_{max}TR) \right] + S_b \left[ L/(2V_{max}TR) - L/[2V_{max}(TR + TE/2)] \right] + S_c L/[2V_{max} (TR + TE/2)] \tag{3.15}
   \]
3.2.2 Gradient Echo

The gradient echo sequence is diagrammed in Figure 3.3.

Gradient echo was developed for the purpose of fast imaging. If TR is shortened to reduce time in conventional spin echo imaging, the signal becomes gradually weaker by a factor of \(1 - e^{-TR/T1}\). Under these circumstances, an RF pulse flip angle less than 90° proves more effective. By reducing the flip angle, \(\theta\), the RF pulse causes only small excursions of the magnetization vector \(M\) (Figure 3.4); and, a steady state is achieved where most of the magnetization remains longitudinal at all times. By this approach, TR can be reduced to tens of milliseconds.
Figure 3.4
Gradient Echo Magnetization Vector

Rapid imaging techniques produce a steady state signal after approximately 20 small flip angle pulses. However, in analyzing flow effects, it is necessary to consider the intermediate response. Gao et al. [21] show the magnetization vector after pulse \( n \) is governed by the following equations:

\[
M_z^{(n)} [\text{TR}] = M_0 \left( 1 - e^{-\frac{\text{TR}}{T_1}} \right) \left( 1 - \cos \theta e^{-\frac{\text{TR}}{T_1}} \right) + M_0 \cos \theta e^{-\frac{\text{TR}}{T_1}} \]
\]

3.16

\[
M_y^{(n)} [\text{TE}] = M_z^{(n-1)} [\text{TR}] \sin \theta e^{-\frac{\text{TE}}{T_2}}
\]

3.17

where:

\( M_z^{(n)} [\text{TR}] = \) the longitudinal magnetization available at the time TR of pulse \( n \).
\( M_y^{(n)}[TE] \) = the transverse magnetization at the time TE of signal echo detection (Assuming a rotating coordinate frame where \( M_x = 0 \) such that \( M_y \) represents the total measured signal.)

Gao et al. [21] extend these equations to predict the total signal \( S_{total} \) available in laminar fluid flow through a cylinder as a function of velocity and fractional volumes as follows: (Equations 3.18-3.22 modified from [21] to be consistent with thesis terminology.)

n-labeled spin populations have entered the slice (L, Figure 3.5) and experienced (n-1) previous pulses. Each population n, for \( n < m \) [where \( m = \) integer value of \( L/(V_{\text{max}} \ TR) \)], occupies the same volume \( (V_{\text{max}}/2) \ TR \pi r^2 \) within the slice (r= radius of the cylinder).

![Figure 3.5](image)

**Figure 3.5**

Fractional Volume Contributions to Gradient Echo Signal
1. IF $V_{\text{max}} = 0$

\[ S_{\text{total}} = M_0 \left( \frac{\sin \theta}{1 - \cos \theta e^{-\frac{TR}{T1}}} \right) (1 - e^{-\frac{TR}{T1}}) e^{-\frac{TE}{T2}} \pi r^2 L \]  

3.18

2. IF $0 < V_{\text{max}} < L/TR$

\[ S_{\text{total}} = \sum_{n=1}^{m} M_{y}^{n}(\text{TE}) \frac{V_{\text{max}}TR \pi r^2 L}{2} + \sum_{k=1}^{N-m} M_{y}^{m+k}(\text{TE}) \Delta m+k \]  

3.19

3. IF $V_{\text{max}} \geq L/TR$

\[ S_{\text{total}} = \sum_{k=1}^{N} M_{y}^{k}(\text{TE}) \Delta k \]  

3.20

where:

$N =$ number of different magnetization populations = equals the number of applied RF pulses

$\Delta m+k$ is the partial volume occupied by $m+k$ labeled spins that remain in the slice for $n > m$:

\[ \Delta m+k = \pi r^2 (V_{\text{max}}TR - \frac{[(m+k)V_{\text{max}}TR - L]^2}{(m+k)V_{\text{max}}TR}) \]  

3.21

\[ \frac{\pi r^2 L^2}{2 V_{\text{max}}TR (m+k)(m+k-1)} \]  

for $k \geq 2$  

3.22

3.3 Theoretical Predictions of Phase Shift Due to Flow in Spin and Gradient Echo Images

This phase shift $\Delta \phi$ along a z-axis magnetic field gradient is defined by the equation:
\[ \Delta \phi = \gamma G_z \Delta z \, t \]  

where:

\( \gamma = \) the gyromagnetic ratio defined in section 3.1 [cycles/sec per Tesla]
\( G_z = \) the magnetic field gradient [Tesla/cm]
\( \Delta z = \) change in distance along the gradient [cm]
\( t = \) duration of the gradient [sec]

Slice select gradients are typically designed to eliminate phase shift with bipolar pulse lobes of equal area (\( A_G \)) and opposite sign as shown in Figure 3.6:

The rephasing lobe compensates for retardation (or acceleration) introduced by the first lobe of \( G_z \). The result is a net phase shift of zero in stationary tissue. However, if there is flow along the slice select gradient, the rephasing lobe will overcompensate (or under compensate) leaving a net phase shift
(\phi_{\text{flow}}) proportional to flow velocity, time before rephasing and the area of the gradient. Dumoulin [8] shows the flow induced phase shift arising from a bipolar gradient pulse is described by:

\[ \phi_{\text{flow}} = \gamma V T A_G \]

where:

- \( V \) = average flow velocity [cm/sec]
- \( T \) = time interval between gradient pulses [sec]
- \( A_G \) = area of each lobe in the gradient pulse [(Tesla/cm)(sec)]
CALCULATION OF EXPERIMENTAL SCAN PARAMETERS

4.1 Initial Conditions

Relaxation times and initial conditions for spin echo and gradient echo calculations were set as follows:

\[ T_{1\,\text{blood}} = 525 \, \text{msec} \, [22] \]
\[ T_{2\,\text{blood}} = 261 \, \text{msec} \, [22] \]
\[ T_{1\,\text{fat}} = 150 \, \text{msec} \, [22] \]
\[ T_{2\,\text{fat}} = 150 \, \text{msec} \, [22] \]
\[ T_{1\,\text{muscle}} = 450 \, \text{msec} \, [22] \]
\[ T_{2\,\text{muscle}} = 64 \, \text{msec} \, [22] \]
\[ L = \text{thickness of Transverse MRI slice} = 1 \, \text{cm} \]
\[ \text{TE} = \text{set to minimize scan time} \]

4.2 Spin Echo: Time of Flight Contrast Enhancement

Theoretical spin echo contrast enhancement for laminar fluid flow through a cylinder (equations 3.12 - 3.15) was programmed (Appendix B) to establish an experimental MRI protocol for imaging arterial and venous blood flow in the major longitudinal vessels of the human abdomen perineum and upper leg.
TE was set at the hardware limit of 25 msec. TR was varied from 50 to 1000 msec to generate a family of signal intensity curves with respect to maximum blood flow velocity ($V_{\text{max}}$). The results for several values of TR are plotted in Figure 4.1

Normalized $S_{\text{total}} = S_{\text{total}} / (M_0 \pi r^2)$.

As TR increases signal intensity increases. This is most pronounced in slow ($V_{\text{max}} = 20$ cm/sec) flow. So, venous flow in the region of interest will be enhanced to a greater extent than abdominal aortic flow by selecting a long (500 or 1000 msec) TR.

![Figure 4.1](image)

**Figure 4.1**

Normalized Signal Intensity versus $V_{\text{max}}$ for varied TR
Additional factors must be taken into account for imaging blood flow. Increasing TR also increases the signal intensity from fat and muscle as shown in Figure 4.2. If blood flow can be enhanced to produce the highest intensity across the image, then (1) vessels stand out clearly in traditional clinical imaging and (2) follow-on computer graphic operations like threshold and maximum projections can be applied.

![Figure 4.2: Effects of TR on Fat and Muscle Signal Intensity](image-url)
Selecting TR= 1000 msec to maximize $S_{total}$ across the full range of $V_{\text{max}}$ in Figure 4.1 would not insure blood flow to have the highest intensity across the transverse MRI slice. At TR= 1000 msec, normalized fat signal intensity (> 0.8) would, in general, exceed the signal intensity from flow. Only blood flow with $V_{\text{max}}$ between 5 and 15 cm/sec would appear brighter.

At the other extreme, TR= 50, blood would appear brighter than both fat and muscle across most of the velocity range; but, the overall image would be depressed in contrast separation of tissues. TR= 200 msec would have limited enhanced blood flow for the range $V_{\text{max}}= 10-40$ cm/sec. TR= 100 msec was chosen for spin echo protocols with expected blood flow enhancement for $V_{\text{max}} > 7$ cm/sec.

4.3 Gradient Echo: Time of Flight Contrast Enhancement

Since the purpose of gradient echo is fast scan imaging, repetition (TR) and echo (TE) times were fixed to the hardware minimum: TR= 20 msec, TE= 11 msec. Equations 3.18 - 3.20 were programmed (Appendix D) to compute the expected signal intensity as a function of maximum blood velocity under varied flip angles, $\theta$. Normalized signal intensity [$S_{\text{total}}/(M_0\pi r^2)$] versus maximum blood flow velocity ($V_{\text{max}}$) is plotted in Figure 4.3 for five flip angles (theta) between 10 and 90 degrees.

At maximum blood flow velocity (90 cm/sec, aorta), the expected signal increases with increasing flip angle. However, at low velocities ($V_{\text{max}} < 30$ cm/sec), increasing flip angle to 60 and 90 degrees decreases signal from theta = 40 degrees.
The expected normalized signal intensity of stationary fat and muscle tissues are computed in the same gradient echo program by setting $V_{\text{max}} = 0$ and changing the respective values for $T1$ and $T2$. Results are presented in Figure 4.4 for theta varied from 10 to 90 degrees.
Comparing Figures 4.3 and 4.4, $\theta = 40^\circ$ provides the widest range of blood flow enhancement over stationary fat tissue. This selection predicts blood flow with $V_{\text{max}} > 5 \text{ cm/sec}$ to be brighter than stationary fat tissue in the image.
4.4 Phase Shift in Spin and Gradient Echo Images

From the theoretical predictions of equation 3.21 ($\phi_{\text{flow}} = \gamma V T A_G$), the expected phase shift due to blood flow traveling perpendicular to an axial MRI slice can be determined by setting:

\[\gamma = \text{gyromagnetic ratio of the proton} = 42.6 \text{ MHz/Tesla}\]
\[V = \text{average velocity} \left(\frac{V_{\text{max}}}{2}\right)\]
\[T = \text{time interval between slice select gradient pulses} = 1 \text{ msec}\]
\[A_G = \text{area of each lobe of the slice select gradient pulse} = 0.000075 \text{ T/cm for 1 msec duration}\]

With $\gamma$, $V$ and $A_G$ fixed, $\phi_{\text{flow}}$ becomes a linear function of velocity as shown in Figure 4.3. Phase shift increases with increased $V_{\text{max}}$.

Actual numerical values of phase shift are acquired through existing hardware and software of the magnet in accordance with the intermediate images presented in Figure 1.7 where phase ($\phi$) is:

\[\phi = \arctan \left(\frac{\text{Imaginary}}{\text{Real}}\right)\]

\[\phi = \arctan \left(\frac{\text{Imaginary}}{\text{Real}}\right)\] 4.1
FIGURE 4.3
Phase Shift versus Maximum Velocity
5 EXPERIMENTAL METHOD

Chapter 4 calculated theoretical MRI scan parameters to enhance the signal from blood flow over that of the surrounding stationary tissue. Actual methods to test the scan protocol and image post-processing operations are detailed in the following sections.

5.1 Subject

The subject for all scan sequences was a 38 year old male graduate student, six feet in height at a weight of 210 pounds, with normal vascular anatomy and circulation.

5.2 Apparatus

The spin echo sequence was performed on the 0.6 tesla Technicare research magnetic resonance imaging system at the Massachusetts General Hospital (MGH) in Boston, MA. Real, Imaginary, Magnitude and Phase were reconstructed using software available on the Technicare research unit; image files were transferred to tape and filmed at the hospital clinical Technicare unit.

The gradient echo sequence was conducted on the 1.5 tesla General Electric Signa clinical magnetic resonance imaging system at McLean Hospital, Belmont, MA. The scan was run under research mode with
parameters selected from the standard options menu whenever possible. Otherwise scan parameters were input manually. Magnitude images were filmed on sight. Original data files were recorded on 9-track magnetic tape and reconstructed into Real, Imaginary, Magnitude and Phase files on a Sun4 workstation at the MGH NMR Computing facility.

No cardiac or respiratory gating instrumentation was used.

5.3 Procedures in Image Acquisition

Each operator was provided a written scan protocol. Technicare parameters used for the spin echo sequences were:

- **Coil:** Body
- **TR:** 100 msec
- **TE:** 20 msec
- **Pulse Sequence:** SE 1
- **Echo Number:** 1 / 1
- **Slice Thickness:** 10.0 mm (1 cm)
- **Field of View:** 48 cm
- **Acquisition:** 256 x 128
- **Number of Averages:** 4
- **Final Image:** 256 x 256
- **Phase encode:** Left - Right

Gradient echo images were acquired as multiple single slices, 1 cm thick with 1 mm spacing between. Center of the acquisition was marked on a median line 4 cm below the umbilicus. Imaging parameters were defined as follows:
Coil: Body
Flip angle: 40°
TR: 20 msec
TE: 11 msec
Pulse Sequence: GRE / 40
Slice Thickness: 10.0 mm (1 cm)
Field of View: 48 cm
Acquisition: 256 x 128
Number of Averages: 4
Final Image: 256 x 256
Phase encode: Left - Right

All scans were performed without flow compensation. Normal clinical MRI procedures were followed. No special instructions were required.

5.4 Procedures in Image Analysis

All image analyses were performed on Sun4 workstations at the Massachusetts Institute of Technology (MIT) Biomedical Imaging Laboratory. Real, Imaginary, Magnitude and Phase files were transferred from MGH to MIT on 9-track magnetic tape. File data was in 2-byte integer format. All manipulations were conducted in C programming as follows: input = short, convert to double for the mathematics then output as character (gray scale 0 to 255). Mathematical file manipulations included one or a combination of the following operations:

For each pixel(i,j) of the final image:

1. computing magnitude and phase from real (Real) and imaginary (Im):
Magnitude \((i,j) = \sqrt{\text{Real}_{i,j}^2 + \text{Im}_{i,j}^2}\)  

2. phase image shifted 180°:

\[
\text{phase}\_180(i,j) = \arctan\left(\frac{\text{Im}_{i,j}}{\text{Real}_{i,j}}\right) + \pi
\]  

3. sum of two images:

\[
\text{sum} (i,j) = \{\text{image}1(i,j) + \text{image}2(i,j)\} / \text{scale}
\]  

where scale limits sum \((i,j)\) to the range 0-255.

4. inversion of a final image:

\[
\text{inverted} (i,j) = 255 - \text{image} (i,j)
\]

Image data manipulation programs are listed as Appendix D. Final image, magnification and viewports were displayed using the TAAC Sun4 demonstration software package IP.
6 RESULTS

6.1 Spin Echo

Spin echo images were acquired under the protocol defined in Chapter 5 for three transverse slices illustrated in Figure 6.1: (A) abdominal aorta - inferior vena cava, (B) common iliac vessels and (C) femoral vessels. Magnitude, phase and magnitude + inverted phase spin echo images are shown in Figure 6.2 through 6.5.

Figure 6.3 (common iliac level) displays the typical magnitude and phase images of the spin echo protocol. Venous flow appeared bright in the magnitude image (6.3B). Right and left common iliac veins are white, near the center of the image medial to their respective psoas major muscles. This agrees with the theoretical calculations of signal from common iliac venous blood flow (0.593 at $V_{\text{max}}$ = 30 cm/sec) being greater than the surrounding tissues (fat = 0.336 and muscle = 0.104). Arteries were black in the magnitude image (6.3B). Common iliac arteries are immediately anterior and slightly lateral to the common iliac veins. Arrow points to the right common iliac artery in figure 6.3B. The magnitude signal intensity for common iliac arterial flow in spin echo images did not agree with the theoretical calculations of 0.355 at $V_{\text{max}}$ = 90 cm/sec. High flow is mapped into the phase image (6.3A), with darker pixel values in vessels with higher $V_{\text{max}}$, as shown by the black common iliac arteries and gray common iliac veins. The combined image of magnitude plus inverted phase displays both arterial and venous flow (6.4A).
Figure 6.3A illustrates several characteristics of the phase image. Space surrounding the body appears as random noise, indiscriminate black and white pixels. Static tissue of the body is uniform and bright across the entire phase image, with the exception of one phase wrap (magnetic field inhomogeneity) which appears at the anterior extreme of the transverse slice. Note the characteristic absence of tissue definition in the phase image (6.3A) as compared to magnitude (6.3B) where fat, bone and muscle are clearly distinct. Major arteries appear black in the phase image. Major veins were gray, darker than static tissues but lighter than the arteries. This image agrees with the increased phase shift with increasing maximum velocity (Figure 4.3) with zero phase shift mapped to image intensity white and maximum phase shift mapped to image intensity black.

This phase mapping is opposite (inverted) to the traditional magnitude (time of flight) images where higher signal intensity from blood flow is mapped into whiter pixel values. To visualize flow, phase was inverted to the magnitude image convention; that is, maximum phase shift was mapped to white.

The combined image of magnitude + inverted phase is shown in Figure 6.4A. Both arterial and venous flow through the slice appear white against the traditional spin echo tissue gray scale. Compare the combined image of 6.4A to the magnitude image of 6.4B. The right common iliac artery (arrow in Figure 6.4A) is clearly defined by flow in the combined image. The common iliac artery in the magnitude image (below) has a comparable intensity (dark) to psoas muscle immediately lateral to the vessel.

The same results are shown in the superior aorta (a, $V_{\text{max}}= 90 \text{ cm/sec}$), inferior vena cava (ivc, $V_{\text{max}}= 20 \text{ cm/sec}$) and hepatic portal vein (h, $V_{\text{max}}= 20 \text{ cm/sec}$) of Figure 6.2. Venous flow is white in the magnitude image.
(Figure 6.2B) while abdominal aorta is dark. Inverting the phase image of the same acquisition and adding to the magnitude produces a combined image (Figure 6.2A) of flow in all three vessels. Note the abdominal aorta (arrow, Figure 6.2A) in combined versus magnitude images.

Figure 6.5 illustrate the same pattern in femoral vessels. Right and left femoral veins ($V_{\text{max}} = 30 \text{ cm/sec}$) are clearly distinct as the brightest pixels in the magnitude image (Figure 6.5B). Femoral arteries ($V_{\text{max}} = 80 \text{ cm/sec}$) immediately lateral to each femoral vein appear dark, similar to muscle. Femoral artery flow is defined by the phase and visualized in the combined image (arrow) in Figure 6.5A. Phase wrap presents a white artifact at the anterior extreme. Otherwise, both arterial and venous flow are mapped as brighter pixel intensity, whiter than static body tissue. Note, muscle and fat layers are retained for landmark identification in the combined image.
Figure 6.1 Transverse Slices

1. Abdominal Aorta
   Inferior Vena Cava

2. Common Iliac

3. Femoral
Fig. 6.2 Spin Echo: Abdominal Aorta - Inferior Vena Cava
A. Magnitude + Inverted Phase  B. Magnitude
Figure 6.3 Spin Echo: Common Iliac
A. Phase           B. Magnitude
Figure 6.4 Spin Echo: Common Iliac
A. Magnitude + Inverted Phase  B. Magnitude
Figure 6.5 Spin Echo: Femoral
A. Magnitude + Inverted Phase  B. Magnitude
6.2 Gradient Echo

Gradient echo images were collected under the protocol defined in Chapter 5 for thirty (30) one cm slices from the abdominal aorta to the profunda femoris vessels; a region described from the line of Figure 6.1A to 4 cm below the line in 6.1C.

The magnitude images are presented in sequential order from superior (Figure 6.6, IMA 001) to inferior (Figure 6.10, IMA 030). Additional notation is provided for orientation (L= left, R= right, A= anterior and P= posterior ). In general, signal intensity was highest (white) in regions of flow; both arteries and veins appeared bright in gradient echo magnitude images. This agreed with the experimental calculations for normalized signal intensity of flow in the major blood vessels (Table C1). For a theta = 40 degrees, blood flow with $V_{max}$ in the range of 20 - 90 cm/sec was determined to give a normalized signal intensity between 0.391 and 0.553, larger than the signal from stationary fat (0.226) and muscle (0.088) tissue.

The abdominal aorta and inferior vena cava are clearly visible in the median plane immediately anterior to the vertebral column in Figure 6.6 Level IMA 002. Moving inferior, the aorta bifurcates at IMA 002; the inferior vena cava begins to divide at level IMA 003 with the left branch obliquely crossing the vertebral column by IMA 005. By level IMA 006, common iliac arteries and veins are visible adjacent to psoas major muscles. The internal iliac artery branches at level IMA 007 (Figure 6.7); below that, both internal iliac arteries and internal iliac veins are intermittent in the magnitude images. The external iliac artery and external iliac vein are definitive, lying beside psoas major from level IMA 010 (Figure 6.7) through 016 (Figure 6.8);
the vein first beginning posteriomedial moving medial to the artery as they become the femoral vessels of the thigh. The great saphenous vein arises from the femoral vein at level IMA 019 (Figure 6.9), dividing into two branches at level 020 and remaining visible in the subcutaneous layer above the muscles throughout the remaining images of Figure 6.9. The femoral artery and vein blur together at the base of the femoral triangle. In the femoral triangle and through the adductor canal, the femoral arteries are either void or blur with the femoral veins which remain bright throughout. Profunda femoris vessels appear dimly at level IMA 022, moving posterior and laterally toward the femur; they become increasingly more visible by level 030 (Figure 6.10).

A typical magnitude and phase image for the gradient echo sequence is presented in Figure 6.11 (common iliac level). Multiple phase wraps are obvious in the raw phase images. While arteries and veins appear bright in the magnitude image, isolated regions of flow can be seen as dark patches in the area of the vessels. This loss of magnitude due to flow appears in the phase image of the same acquisition. The right common iliac artery of Figure 6.11A appears dark. The corresponding phase image (Figure 6.11B, arrow) maps the phase shift due to flow in the right common iliac artery to black. Note the magnitude signal lost in the center of the right common iliac vein immediately posterior to the artery in Figure 6.11A. The corresponding center is mapped into the phase image of Figure 6.11B. Flow can also be seen in the phase for left common iliac artery and elongated center of the right common iliac vein.

Flow in the major vessels is better visualized by the combination of magnitude + inverted phase. Combination images for the aorta, inferior vena cava and common iliac vessels are shown in Figures 6.12 and 6.13.
Arrows (6.12B and 6.13B) note the enhancement of flow information from inverted phase that is lost in the corresponding magnitude images (6.12A and 6.13A).
Figure 6.6 Gradient Echo: Magnitude Levels 001-006
Figure 6.7 Gradient Echo: Magnitude Levels 007-012
Figure 6.8 Gradient Echo: Magnitude Levels 013-018
Figure 6.9  Gradient Echo: Magnitude Levels 019–024
Figure 6.10  Gradient Echo: Magnitude Levels 025–030
Figure 6.11 Gradient Echo: Common Iliac
A. Magnitude    B. Phase
Figure 6.12 Gradient Echo: Abdominal Aorta-Inferior Vena Cava
A. Magnitude
B. Magnitude + Inverted Phase
Figure 6.13 Gradient Echo: Common Iliac
A. Magnitude  B. Magnitude + Inverted Phase
7 DISCUSSION

The longitudinal vessels of the human abdomen, perineum and upper leg can be isolated from static tissue by maximizing time-of-flight techniques for magnitude and including the phase information available in the same MRI slice acquisition.

Time-of-flight effects were predominant in fast gradient echo scans with TR= 20 msec, TE= 11 msec. Bright blood flow appeared in the aorta, common iliac, external iliac, internal iliac, femoral and profunda femoris arteries. Venous blood flow was also bright for vena profunda femoris, saphenous, femoral, external iliac, internal iliac and common iliac veins as well as the inferior vena cava and hepatic portal vein. Increased magnitude was consistent for both arteries and veins with isolated exceptions. Blood flow in the gradient echo images appeared brighter than static tissue. This image agreed with theoretical calculations.

Time-of-flight enhancement under spin echo imaging (TR= 100 msec, TE= 20 msec) was limited to venous flow. Veins were bright but arteries were dark in the spin echo magnitude image. Theoretical calculations for laminar blood flow had predicted intensity to fall with the higher \( V_{\text{max}} \) of the aorta, common iliac and femoral arteries, but to stay above the intensity levels of static tissue. Actual spin echo arterial flow magnitude values fell below the intensity of fat to gray scale approximating muscle.

Phase effects compensated for the loss of magnitude information. This was most apparent in high arterial flow velocity in spin echo images. Higher \( V_{\text{max}} \) that diminished magnitude mapped a shift in the intermediate phase
image that darkened in intensity with increasing velocity. Major artery lumen appeared black while veins were dark gray against a uniform white field of static tissue. The same effects were seen in gradient echo images. The intermittent regions of low magnitude intensity in the vessel lumen of gradient echo magnitude images corresponded to an increase in darkness (phase shift) in the phase image at the same pixel location.

Inverting the phase image presented flow information in the traditional bright blood format. Since phase and magnitude represented intermediate images of the same data acquisition, a pixel by pixel combination of magnitude plus inverted phase provide a complete angiogram for blood flow in major arteries and veins through the slice. Flow information lost in the time-of-flight magnitude image was regained by addition of inverted phase. The combined image gained qualities of both intermediate images: (1) gray scale discrimination of blood flow and body tissues from magnitude and (2) flow information from phase.

Phase wrap limited the combined intermediate image approach. In spin echo images, phase wrap appeared in a single horizontal line. In gradient echo images, several wraps radiated across the phase image. Inverting an image with phase wrap generates a maximum intensity artifact limiting additional computer graphic operations (like 3-D maximum projection) to the immediate regions surrounding the vessels. Phase wrap involves hardware generation of inhomogenous fields and software misinterpretation in crossing lines of trigonometric discontinuity. This is an ongoing problem with magnetic resonance phase imaging, and, a continued focus in magnet software and hardware research. The most promising research work appears in the combination of hardware and software design to
limit phase shift from gradients to less than 1 radian. Success in this design could lead to clinical MRI quantification of blood flow.

There are several advantages to the combined intermediate image angiography approach:

1. The phase enhanced time-of-flight image generates a complete angiogram of arterial and venous flow through major vessels of the slice in a single data acquisition.

2. The combined image maintains soft tissue definition, presenting blood flow among the highest intensities of the image. All structures are retained. This provides clear identification from anatomical relations. For example, common iliac vessels adjacent to psoas major muscle. Retaining tissue dependent gray scales also allows for continued computer graphic operations from simple threshold algorithms to elaborate ray tracing routines for numerous display options.

3. Single acquisition prevents spatial misregistration. Multiple intermediate images can be combined on a pixel by pixel basis. And, in general, any post-processing algorithms that maintain pixel location could be used as operators on the image set.

4. Patient time in the magnet is minimized.

5. Phase enhanced time-of-flight imaging relies on velocity of blood flow through the slice. No cardiac or respiratory gating is required.
6. Spin echo and gradient echo imaging are standard clinical MRI protocols with sequence parameters input at the operator console. No special coils or instrumentation are used. Special flow compensation protocols were not required.

The thesis demonstrated normal blood flow MRI angiography from intermediate images in spin echo and gradient echo protocols. The implied next step would be to evaluate the technique as a diagnostic tool. Inversion of phase and addition of images consume little computer time and space. Since intermediate images are available in MRI system memory, the same off-line work station algorithms could be programmed as an operator menu option.

Additional topics exist for the role of phase enhanced time-of-flight magnetic resonance images in computer graphics. This procedure suggests reformatting the series transverse planes into a volume data set for 3-D threshold isolation for complete vascular tree of the major arteries and veins the human abdomen, perineum and upper leg. Application of ray tracing with transparencies could add surrounding body structures retained by the acquisition. Current instrumentation would probably require graphical extraction of the phase flow information away from the artifact of phase wrap. But, with ongoing improvements in imaging magnets, the algorithm of magnitude + inverted phase presented may very well suffice as the clinical MRI angiogram.
REFERENCES


22. Clark JA. The magnetic resonance signal and its generation. Figure 38. *Magnetic Resonance Imaging Visiting Fellowship Course*, Massachusetts General Hospital, Department of Radiology, September 12-16, 1988.

APPENDIX A

Velocity Relations in Laminar Flow

For laminar flow through a cylindrical vessel, the average velocity ($V_{avg}$) can be shown to be $1/2$ the maximum axial velocity ($V_{max}$). Consider a cylindrical unit of liquid of length $L$ and radius $r$. The viscous force ($F_{viscous}$) retarding the motion of the cylindrical liquid unit is the area of its surface ($2\pi rL$) times its kinematic viscosity ($\mu$) times the velocity gradient across the tube ($\frac{dv}{dr}$):

$$F_{viscous} = (2\pi rL)\mu \frac{dv}{dr} \quad \text{(A1.1)}$$

The force over the cross-sectional area of the cylinder ($\pi r^2$) exerted by the pressure at the ends of the cylinder ($P_1$ and $P_2$) is:

$$F_{pressure} = \pi r^2(P_1 - P_2) \quad \text{(A1.2)}$$

Under Newtonian conditions, the forces are equal and opposite so that:

$$\pi r^2(P_1 - P_2) = -(2\pi rL)\mu \frac{dv}{dr} \quad \text{(A1.3)}$$

$$\therefore \quad \frac{dv}{dr} = \frac{r(P_1 - P_2)}{2L\mu} \quad \text{(A1.4)}$$

by integration:

$$v = \frac{r^2(P_1 - P_2)}{4L\mu} + C \quad \text{(A1.5)}$$

Enforcing the boundary condition that fluid velocity at the wall is zero; that is, for $r=R$, $v=0$, then:

$$C = \frac{R^2(P_1 - P_2)}{4L\mu} \quad \text{(A1.6)}$$
and:

\[ v = \frac{r^2 (P_1 - P_2)}{4L\mu} + \frac{R^2 (P_1 - P_2)}{4L\mu} = \frac{(R^2 - r^2)(P_1 - P_2)}{4L\mu} \quad \text{A1.7} \]

which is the equation for a parabola with \( v = 0 \) when \( r=R \) and \( v = V_{\text{max}} \) at \( r=0 \).

The volume flow rate \( Q \) is computed from the solid of revolution:

\[
Q = \int_0^r 2\pi vr \, dr \quad \text{A1.8}
\]

substituting for \( v \):

\[
Q = \frac{2\pi (P_1 - P_2)}{4L\mu} \int_0^r (R^2 - r^2) \, dr = \frac{\pi (P_1 - P_2) R^4}{8L\mu} \quad \text{A1.9}
\]

Generally units are: \( Q = \text{cm}^3/\text{sec} ; P = \text{dynes/cm}^2 \); \( R, r \) and \( L \) in cm; \( \mu \) in poise (poise = 1 dyne-sec/cm²)

From equation A1.5 the maximum velocity (\( r=0 \)) is:

\[
V_{\text{max}} = \frac{(P_1 - P_2) R^2}{4\mu L} \quad \text{A1.10}
\]

The average velocity (\( V_{\text{avg}} \)) across the cylinder is found by dividing the volume flow by the cross-sectional area:

\[
V_{\text{avg}} = \frac{\pi(P_1 - P_2) R^4}{8\mu L \cdot \pi R^2} = \frac{(P_1 - P_2) R^2}{8\mu L} \quad \text{A1.11}
\]

So, the average velocity is \( 1/2 \) \( V_{\text{max}} \).
APPENDIX B

Spin Echo Flow Enhancement Calculations

Sample Basic Spin Echo program for the computation of normalized MRI signal intensity based on parabolic blood fluid flow through a rigid cylinder. TE set at 20 msec, example TR= 1 sec (1000 msec).

OPEN "se1000out" FOR OUTPUT AS #2
  te=.02: tr=1!
  t1=.525: t2=.261
  L= 1!
  FOR vmax= 0 TO 100 STEP 5
    CALL FindMy(vmax)
  NEXT
CLOSE #2
END

SUB FindMy(vmax) STATIC
  SHARED tr,te,t1,t2,L
  difm=tr-(te/2)
  difs=tr+(te/2)
  sa= EXP(-te/t2)
  sb= (1-(2*EXP(-difm/tl)))*EXP(-te/t2)
  sc= (1-(2*EXP(-difm/tl))+EXP(-tr/tl))*EXP(-te/t2)
  IF vmax >= 0! AND vmax <= (L/difs) THEN CALL
    sig1(sa,sb,sc,difm,difs,vmax)
  IF vmax > (L/difs) AND vmax <= (L/tr) THEN CALL
    sig2(sa,sb,sc,difm,difs,vmax)
  IF vmax > (L/tr) AND vmax <= (L/(te/2)) THEN CALL
    sig3(sa,sb,sc,difm,difs,vmax)
  IF vmax > (L/(te/2)) THEN CALL
    sig4(sa,sb,sc,difm,difs,vmax)
END SUB

SUB sig1(sa,sb,sc,difm,difs,vmax) STATIC
  SHARED L,te,tr
  a= vmax*difm/(2*L)
  b= vmax*te/(4*L)
  c= 1- (vmax*difs/(2*L))
  signal= (sa*a) + (sb*b) + (sc*c)
  WRITE #2, signal
END SUB
SUB sig2(sa, sb, sc, difm, difs, vmax) STATIC
SHARED L, te, tr
a = vmax*difm/(2*L)
b = 1-(L/(2*vmax*difs))-(vmax*tr/(2*L))
c = L/(2*vmax*difs)
signal = (sa*a) + (sb*b) + (sc*c)
WRITE #2, signal
END SUB

SUB sig3(sa, sb, sc, difm, difs, vmax) STATIC
SHARED L, te, tr
a = 1-(L/(2*vmax*tr))-(vmax*te/(4*L))
b = (L/(2*vmax*tr))-(L/(2*vmax*difs))
c = L/(2*vmax*difs)
signal = (sa*a) + (sb*b) + (sc*c)
WRITE #2, signal
END SUB

SUB sig4(sa, sb, sc, difm, difs, vmax) STATIC
SHARED L, te, tr
a = (L/(vmax*te))-(L/(2*vmax*tr))
b = (L/(2*vmax*tr))-(L/(2*vmax*difs))
c = L/(2*vmax*difs)
signal = (sa*a) + (sb*b) + (sc*c)
WRITE #2, signal
END SUB
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**TABLE B1**

Calculated Normalized Signal Intensity (S _total_ ) from Spin Echo Program [TE= 20 msec]
Appendix C

Gradient Echo Flow Enhancement Calculations

Sample program for calculating Gradient Echo Maximum Signal Intensity from blood flow. Results listed in Table C1.

OPEN "ge40out" FOR OUTPUT AS #2
tr=.02:te= .011
t1=.525: t2=.261
Length =1!
theta= 40

nmax = 128

DEF FNc1 (angler) = SIN(angler)
DEF FNc2 (angler) = 1-(COS(angler) * EXP(-tr/t1))
DEF FNc3 = (1-EXP(-tr/t1))*EXP(-te/t2)
DEF FNc1 My = 1-EXP(-tr/t1)
DEF FNc2 My (angler,n)= 1-((COS(thetar))^(n-1))*EXP(-(n-1)*tr/t1))
DEF FNc3 My (angler,n)= 1-(COS(thetar)*EXP(-tr/t1))
DEF FNc4 My (angler,n)=
   ((COS(thetar))^(n-1)) *EXP(-(n-1)*tr/t1)*(SIN(thetar)*EXP(-te/t2))

FOR vmax= 0 TO 100 STEP 5
    thetar= theta/57.29578
    IF vmax = 0 THEN m=1 ELSE m= INT(Length/(vmax*tr))
    IF vmax=0 THEN
        sum1 = FNc1(thetar)*FNc3*Length/FNc2(thetar)
        REM WRITE #2, vmax,sum1
        WRITE #2, sum1
    END IF
    IF vmax > 0 AND vmax < = (Length/tr) THEN
        flowm= 0!:summy= 0!:part1= 0!: part2= 0!: sump= 0!
        FOR n=1 TO m STEP 1
            cmy= (FNc1 My*FNc2 My (thetar,n)/FNc3 My (thetar,n)) +
                FNc4 My (thetar,n)
            flowm=cmy*vmax*tr*Length/2
            summy=summy+flowm
        NEXT n
mpl = m + 1
vmtr = vmax * tr

cmpl1 =
(FNc1My * FNc2My (thetar, mp1) / FNc3My (thetar, mp1)) +
FNc4My (thetar, mp1)

top = ((mp1 * vmtr) - Length)^2!
bottom = mp1 * vmtr
del1 = (vmtr - (top/bottom))/2!
part1 = cmpl1 * del1

FOR k = 2 TO (nmax - m) STEP 1
  mpk = m + k
  cmp2 =
  (FNc1My * FNc2My (thetar, mpk) / FNc3My (thetar, mpk)) +
  FNc4My (thetar, mpk)
  del2 = (Length^2) / (2 * vmtr * (m+k)*(m+k-1))
  part2 = part2 + (cmp2 * del2)
NEXT k

parts = part1 + part2
sum = sum + parts

REM WRITE #2, vmax, sum
WRITE #2, sum
END IF

IF vmax > (Length/tr) THEN
  part1 = 0!: part2 = 0!: sum = 0!
  vmtr = vmax * tr
  j = 1!

  cmpl = (FNc1My * FNc2My (thetar, j) / FNc3My (thetar, j)) +
  FNc4My (thetar, j)

top = (vmtr - Length)^2!
bottom = vmtr
del1 = (vmtr - (top/bottom))/2!
part1 = cmpl1 * del1

END IF
FOR j=2 TO (nmax) STEP 1
    del2 = (Length^2)/(2*vmtr*(m+j)*(m+j-1))
    cm2 = (FNc1My*FNc2My (thetar,j)/FNc3My (thetar,j)) +
          FNc4My (thetar,j)
    part2 = part2 + (cm2*del2)
NEXT j

    sum = part1 + part2
    REM WRITE #2, vmax,sum
    WRITE #2, sum
END IF
NEXT vmax

CLOSE #2

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<td>0.3910913</td>
<td>0.3408042</td>
<td>0.221284</td>
</tr>
<tr>
<td>25</td>
<td>0.2432572</td>
<td>0.3391304</td>
<td>0.4206007</td>
<td>0.3916536</td>
<td>0.2674246</td>
</tr>
<tr>
<td>30</td>
<td>0.2326155</td>
<td>0.337716</td>
<td>0.4438773</td>
<td>0.4352627</td>
<td>0.3135408</td>
</tr>
<tr>
<td>35</td>
<td>0.2246037</td>
<td>0.3366187</td>
<td>0.4622811</td>
<td>0.4720304</td>
<td>0.3596432</td>
</tr>
<tr>
<td>40</td>
<td>0.2182361</td>
<td>0.3357197</td>
<td>0.4776396</td>
<td>0.5045221</td>
<td>0.4057368</td>
</tr>
<tr>
<td>45</td>
<td>0.2129642</td>
<td>0.3349528</td>
<td>0.4909678</td>
<td>0.5341632</td>
<td>0.4518247</td>
</tr>
<tr>
<td>50</td>
<td>0.2084596</td>
<td>0.3342785</td>
<td>0.5028749</td>
<td>0.5618091</td>
<td>0.4979085</td>
</tr>
<tr>
<td>55</td>
<td>0.2046435</td>
<td>0.333699</td>
<td>0.5131825</td>
<td>0.586216</td>
<td>0.5398014</td>
</tr>
<tr>
<td>60</td>
<td>0.2014634</td>
<td>0.3332161</td>
<td>0.5217723</td>
<td>0.606555</td>
<td>0.5747121</td>
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<tr>
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<td>0.1987724</td>
<td>0.3328076</td>
<td>0.5290406</td>
<td>0.6237649</td>
<td>0.604252</td>
</tr>
<tr>
<td>70</td>
<td>0.196466</td>
<td>0.3324575</td>
<td>0.5352706</td>
<td>0.6385164</td>
<td>0.6295719</td>
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<tr>
<td>75</td>
<td>0.194467</td>
<td>0.3321541</td>
<td>0.54067</td>
<td>0.651301</td>
<td>0.6515187</td>
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<td>0.3318884</td>
<td>0.5453941</td>
<td>0.6624875</td>
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<tr>
<td>85</td>
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<td>0.3316541</td>
<td>0.5495628</td>
<td>0.6723579</td>
<td>0.6876586</td>
</tr>
<tr>
<td>90</td>
<td>0.1898028</td>
<td>0.3314458</td>
<td>0.5532682</td>
<td>0.6811316</td>
<td>0.7027181</td>
</tr>
<tr>
<td>95</td>
<td>0.1885753</td>
<td>0.3312595</td>
<td>0.5565836</td>
<td>0.6889817</td>
<td>0.7161924</td>
</tr>
<tr>
<td>100</td>
<td>0.1874707</td>
<td>0.3310918</td>
<td>0.5595673</td>
<td>0.6960469</td>
<td>0.7283193</td>
</tr>
<tr>
<td>Fat</td>
<td>0.146</td>
<td>0.223</td>
<td>0.226</td>
<td>0.179</td>
<td>0.116</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.110</td>
<td>0.124</td>
<td>0.088</td>
<td>0.061</td>
<td>0.037</td>
</tr>
</tbody>
</table>

**Table C1**

Calculated Normalized Signal Intensity (S total) from
Gradient Echo Program [TR= 20 msec, TE = 11 msec]
Appendix D
Image Postprocessing Routines

#include <stdio.h>
#include <math.h>
#define IMGLENX 256
#define IMGLENY 256
#define LENGTH IMGLENX*IMGLENY

main(argc, argv) 
  int argc;
  char *argv[];
{
  int i=0;
  short re_img[LENGTH], im_img[LENGTH];
  double phase[LENGTH], phase_180[LENGTH], mag[LENGTH];
  double gradx[LENGTH], grady[LENGTH];
  double gradx_180[LENGTH], grady_180[LENGTH];
  double maggrad[LENGTH], maggrad_180[LENGTH];
  double min_abs_maggrad[LENGTH];
  double x, y, angle;
  double maxp=-100.0, minp= 100.0;
  double maxm=-100.0, minm= 100.0;
  double max_gradx=-100.0, min_gradx= 100.0;
  double max_gradx_180=-100.0, min_gradx_180= 100.0;
  double max_grady=-100.0, min_grady= 100.0;
  double max_grady_180=-100.0, min_grady_180= 100.0;
  double max_absgrad=-100.0, min_absgrad= 130.0;
  double maxm=100.0, minm= 100.0;
  double max_gradx=-100.0, min_gradx= 100.0;
  double max_gradx_180=-100.0, min_gradx_180= 100.0;
  double max_grady=-100.0, min_grady= 100.0;
  double max_grady_180=-100.0, min_grady_180= 100.0;
  double max_absgrad=-100.0, min_absgrad= 130.0;
  double scalep, scalem, scale_gradx, scale_grady, scale_maggrad;
  double sumsq, sumgrad, sumgrad_180;
  unsigned char phase_c, phase_180c, phase_maxc, phase_ic, mag_c;
  unsigned char gradx_c, gradx_180_c, grady_c, grady_180_c;
  unsigned char maxc, maggradc,maggrad_180_c, min_absmaggrad_c;
  if (argc < 3){
    printf("ln Usage phase Real in Imaginary in\n\n");
    exit(0);
  }

  fpr = fopen(argv[1], "r");
  fpl = fopen(argv[2], "r");
  fpop1 = fopen("PHASE", "w");
  fpop2 = fopen("PHASE180", "w");
  fpop3 = fopen("PHASE_MAX", "w");
  fpop4 = fopen("PHASE_0", "w");
  fpm = fopen("MAG", "w");
  fpox = fopen("GRADX", "w");
  fpox2 = fopen("GRADX_180", "w");
  fpoy = fopen("GRADY", "w");
  fpoy2 = fopen("GRADY_180", "w");
  fpom = fopen("MAGGRAD", "w");
  fpom2 = fopen("MAGGRAD_180", "w");
  fpomg = fopen("A_MAGGRAD", "w");
  fread(&re_img[0], sizeof(short), LENGTH, fpr);
  fread(&im_img[0], sizeof(short), LENGTH, fpr);

Open files for read & write

Read real & imaginary images
for (i=0; i< LENGTH; i++) {
  x= (double) reimg[i];
  y= (double) imimg[i];
  if((x==0.0) && (y==0.0)) x= 1.0;
  angle= atan2(y,x);
  if(angle >= 0.0)
    phase[i] = angle;
  if(angle < 0.0)
    phase[i] = angle + 6.2831853;
  phase_180[i] = angle + 3.141593;
  if(phase[i] > maxp) maxp= phase[i];
  if(phase[i] < minp) minp= phase[i];
  sumsq= (x*x) + (y*y);
  mag[i]= sqrt(sumsq);
  if(mag[i] > maxm) maxm= mag[i];
  if(mag[i] < minm) minm= mag[i];
}
/* the last column is not technically correct here */
for(i=0; i< LENGTH-1; i++)
  gradx[i]= phase[i+1] - phase[i];
  gradx_180[i]= phase_180[i+1] - phase_180[i];
  if(gradx[i] > max_gradx) max_gradx= gradx[i];
  if(gradx[i] < min_gradx) min_gradx= gradx[i];
  if(gradx_180[i] > max_gradx_180) max_gradx_180= gradx_180[i];
  if(gradx_180[i] < min_gradx_180) min_gradx_180= gradx_180[i];

gradx[LENGTH]= gradx[LENGTH-1];
gradx_180[LENGTH]= gradx_180[LENGTH-1];
for(i=0; i< LENGTH-IMGLENX; i++)
  grady[i]= phase[i+IMGLENX] - phase[i];
  grady_180[i]= phase_180[i+IMGLENX] - phase_180[i];
  if(grady[i] > max_grady) max_grady= grady[i];
  if(grady[i] < min_grady) min_grady= grady[i];
  if(grady_180[i] > max_grady_180) max_grady_180= grady_180[i];
  if(grady_180[i] < min_grady_180) min_grady_180= grady_180[i];
/* for the last row duplicates the row above */
for(i=IMGLENX; i< LENGTH; i++)
  grady[i]= grady[i-IMGLENX];
  if(grady[i] > max_grady) max_grady= grady[i];
  if(grady[i] < min_grady) min_grady= grady[i];
  if(grady_180[i] > max_grady_180) max_grady_180= grady_180[i];
  if(grady_180[i] < min_grady_180) min_grady_180= grady_180[i];

for(i=0; i< LENGTH; i++)
  sumgrad= (gradx[i]*gradx[i]) + (grady[i]*grady[i]);
  sumgrad_180= (gradx_180[i]*gradx_180[i]) + (grady_180[i]*grady_180[i]);
  maggrad[i]= sqrt(sumgrad);
  maggrad_180[i]= sqrt(sumgrad_180);
  if(maggrad[i] > max_maggrad) max_maggrad= maggrad[i];
  if(maggrad[i] < min_maggrad) min_maggrad= maggrad[i];
  if(maggrad_180[i] > max_maggrad_180)
    max_maggrad_180= maggrad_180[i];
  if(maggrad_180[i] < min_maggrad_180)
    min_maggrad_180= maggrad_180[i];

97
\[ \text{min_maggrad_180} = \text{maggrad_180}[i]; \]

\[ \text{a_maggrad}[i] = \text{fabs(maggrad}[i]); \]
\[ \text{a_maggrad_180}[i] = \text{fabs(maggrad_180}[i]); \]

\[
\begin{aligned}
\text{if}(\text{a_maggrad}[i] < \text{a_maggrad_180}[i]) \\
& \quad \text{min_abs_maggrad}[i] = \text{a_maggrad}[i]; \\
\text{else} \\
& \quad \text{min_abs_maggrad}[i] = \text{a_maggrad_180}[i];
\end{aligned}
\]

\[
\begin{aligned}
\text{if}(\text{min_abs_maggrad}[i] > \text{max_absgrad}) \\
& \quad \text{max_absgrad} = \text{min_abs_maggrad}[i]; \\
\text{if}(\text{min_abs_maggrad}[i] < \text{max_absgrad}) \\
& \quad \text{min_absgrad} = \text{min_abs_maggrad}[i];
\end{aligned}
\]

\[
\begin{aligned}
\text{printf("
\text{maxp}= \%f
\text{minp}= \%f
\text{maxm}= \%f
\text{minm}= \%f
\text{max_gradx}= \%f
\text{min_gradx}= \%f
\text{max_gradx_180}= \%f
\text{min_gradx_180}= \%f
\text{max_grady}= \%f
\text{min_grady}= \%f
\text{max_grady_180}= \%f
\text{min_grady_180}= \%f
\text{max_maggrad}= \%f
\text{min_maggrad}= \%f
\text{max_maggrad_180}= \%f
\text{min_maggrad_180}= \%f
\text{max_absgrad}= \%f
\text{min_absgrad}= \%f
\text{scalep}= \text{(maxp - minp)} / 255.0; \\
\text{scalem}= \text{(maxm - minm)} / 255.0; \\
\text{scale_gradx}= \text{(max_gradx - min_gradx)} / 255.0; \\
\text{scale_grady}= \text{(max_grady - min_grady)} / 255.0; \\
\text{scale_gradx_180}= \text{(max_gradx_180 - min_gradx_180)} / 255.0; \\
\text{scale_grady_180}= \text{(max_grady_180 - min_grady_180)} / 255.0; \\
\text{scale_absgrad}= \text{(max_absgrad - min_absgrad)} / 255.0; \}
\end{aligned}
\]

\[
\begin{aligned}
\text{for}(i=0; i<\text{LENGTH}; i++) \\
& \quad \text{phase_c} = (\text{unsigned char})((\text{phase}[i]-\text{minp})/\text{scalep}); \\
& \quad \text{phase_180c} = (\text{unsigned char})((\text{phase_180}[i]-\text{minp})/\text{scalep}); \\
& \quad \text{if}(\text{phase_180c} > \text{phase_c}) \\
& \quad \quad \text{phase_maxc} = \text{phase_180c}; \\
& \quad \text{else} \text{phase_maxc} = \text{phase_c}; \\
& \quad \text{mag_c} = (\text{unsigned char})((\text{mag}[i]-\text{minm})/\text{scalem}); \\
& \quad \text{gradx_c} = (\text{unsigned char})((\text{gradx}[i]-\text{min_gradx})/\text{scale_gradx}); \\
& \quad \text{gradx_180_c} = (\text{unsigned char})((\text{gradx_180}[i]-\text{min_gradx_180})/\text{scale_gradx_180}); \\
& \quad \text{grady_c} = (\text{unsigned char})((\text{grady}[i]-\text{min_grady})/\text{scale_grady}); \\
& \quad \text{grady_180_c} = (\text{unsigned char})((\text{grady_180}[i]-\text{min_grady_180})/\text{scale_grady_180}); \\
& \quad \text{maggrad_c} = (\text{unsigned char})((\text{maggrad}[i]-\text{min_maggrad})/\text{scale_maggrad}); \\
& \quad \text{maggrad_180_c} = (\text{unsigned char})((\text{maggrad_180}[i]-\text{min_maggrad_180})/\text{scale_maggrad}); \\
& \quad \text{min_abs_maggrad_c} = (\text{unsigned char})((\text{min_abs_maggrad}[i]-\text{min_absgrad})/\text{scale_absgrad});
\end{aligned}
\]
putc(phase_c, fpop1);
putc(phase_180c, fpop2);
putc(phase_maxc, fpop3);
putc(phase_ic, fpop4);
putc(mag_c, fpom);
putc(gradx_c, fpox);
putc(gradx_180c, fpox2);
putc(grady_c, fpoy);
putc(grady_180_c, fpoy2);
putc(maggrad_c, fpomg);
putc(maggrad_180_c, fpomg2);
putc(min_abs_maggrad_c, fpomg);
fclose(fpop1);
fclose(fpop2);
fclose(fpom);
fclose(fpox);
fclose(fpoy);
fclose(fpomg);
fclose(fpomg2);
fclose(fpomg);
}

Output to files

END
Add two images and output their sum.

```c
#include <stdio.h>
#include <math.h>
#define IMGLENX 256
#define IMGLENY 256
#define LENGTH IMGLENX * IMGLENY

main(argc, argv)
int argc;
char *argv[];
{
    FILE *fpl, *fp2, *fpo;
    int i;
    unsigned char image1[LENGTH];
    unsigned char image2[LENGTH];
    double new_image[LENGTH];
    double maxnew=100.0, minnew=100.0;
    double scalenew;
    unsigned char new_image_c;

    if (argc < 3) {
        printf("\n Usage conv3x3 image1 image2 new_image\n\n");
        exit(0);
    }

    fpl= fopen(argv[1], "r");
    fp2= fopen(argv[2], "r");
    fpo= fopen("ADDOUT", "w");

    fread(image1, sizeof(char), LENGTH, fpl);
    fread(image2, sizeof(char), LENGTH, fp2);

    for (i=0; i<LENGTH; i++) {
        new_image[i]= image1[i] + image2[i];
        if(new_image[i] > maxnew) maxnew= new_image[i];
        if(new_image[i] < minnew) minnew= new_image[i];
    }

    printf("\n maxnew= %f\n", maxnew);
    printf(" minnew= %f\n", minnew);
    scalenew= (maxnew - minnew) / 255.0;

    for (i=0; i<LENGTH; i++)
        new_image_c= (unsigned char)((new_image[i]-minnew)/scalenew);
       putc(new_image_c, fpo);
}
fclose(fpo);
fclose(fpl);
fclose(fp2);
}``
Add one image to the inverted second image. Output their sum.

#include <stdio.h>
#include <math.h>
#define IMGLENX 256
#define IMGLENY 256
#define LENGTH IMGLENX * IMGLENY

main(argc, argv)
int argc;
char *argv[];
{
int i;
unsigned char imagel[LENGTH];
unsigned char image2[LENGTH];
unsigned char image2_i[LENGTH];
unsigned char max_im2= 0;
double new_image[LENGTH];
double maxnew=-100.0, minnew= 100.0;
double scalenew;
unsigned char new_imagec;
if (argc < 3){
  printf("-n Usage conv3x3 image new_image

");
  exit(0);
}

fpl= fopen(argv[1], "r");
fp2= fopen(argv[2], "r");
fpo= fopen("ADDOUTI", "w");
fread(&imagel[0], sizeof(char), LENGTH, fpl);
fread(&image2[0], sizeof(char), LENGTH, fp2);
for (i=0; i< LENGTH; i++)
  if(image2[i] > maxim2) maxim2= new_image[i];
for (i=0; i< LENGTH; i++)
  image2_i[i]= maxim2 - image2[i];
for (i=0; i< LENGTH; i++)
  new_image[i]= imagel[i] + image2_i[i];
  if(new_image[i] > maxnew) maxnew= new_image[i];
  if(new_image[i] < minnew) minnew= new_image[i];

printf("-n maxnew= %f\n",maxnew);
printf("-n minnew= %f\n",minnew);

scalenew= (maxnew - minnew) / 255.0;

for(i=0; i<LENGTH; i++){
    new_imagec= (unsigned char) ((new_image[i]-minnew)/scalenew);
    putc(new_imagec, fpo);
}

fclose(fpo);
fclose(fp1);
fclose(fp2);
}