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Los Angeles

Variable Flip Angle Balanced Steady State Free Precession MRI

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy
in Biomedical Engineering

by

Subashini Srinivasan

2014

ABSTRACT OF THE DISSERTATION

Variable Flip Angle Balanced Steady State Free Precession MRI

by

Subashini Srinivasan

Doctor of Philosophy in Biomedical Engineering

University of California, Los Angeles, 2014

Professor Daniel B. Ennis, Chair

Cardiac cine imaging for conscious pediatric patients and patients with respiratory and/or cardiac dysfunction is challenging due to the need for repeated, reproducible, and sometimes prolonged breath holds. Hence a free-breathing cardiac cine exam is essential for improved patient comfort. Cardiac cine exams are routinely performed using balanced steady-state free precession (bSSFP) imaging due to its high signal-to-noise ratio (SNR) efficiency. However, bSSFP imaging requires the use of a high flip angle for increased signal and a short repetition time to reduce image artifacts. These two requirements result in increased heat energy deposition, measured in specific absorption rate (SAR), in units of Watts per unit mass of the patient's weight (W/kg). FDA regulates SAR in order to ensure patient safety during MRI exams. As such the increased SAR that accords with using bSSFP can limit its application at higher field strengths ($\geq 3T$).

High SAR also poses the highest risk for RF induced lead-tip heating and potential tissue damage and may inhibit pacing and/or ICD shocks in patients with implanted pacemakers or ICDs. Hence, performing cardiac cine imaging with lower SAR bSSFP is essential for safe imaging of patients with devices as well as to minimize patient discomfort.

3D T_2 weighted spin echo imaging is another SAR intensive pulse sequence due to the use of large flip angles. Extending the acquisition duration can reduce the sequence's SAR. As a consequence, 3D T_2 weighted prostate imaging takes ~7 minutes to acquire, which leads to patient discomfort as well as increased sensitivity to motion artifacts.

In this dissertation, variable flip angle (VFA) bSSFP techniques have been developed to lower the SAR or improve the signal and contrast of bSSFP for free-breathing cardiac cine applications, 3D T_2 weighted prostate imaging and non-contrast MR arteriography of the lower leg all with the aim of reducing patient discomfort while maintaining image quality.

The first objective was to determine the optimal bSSFP FA for cardiac cine imaging. Detailed Bloch simulations of stationary myocardium, flowing blood in the presence of imperfect slice profile and off-resonance effects were simulated and compared with in vivo imaging experiments of ten healthy subjects and seven patients with a range of ejection fraction and heart rate. The in vivo imaging in healthy subjects and clinical patients show that high blood-myocardium contrast can be obtained with a FA $\sim 105^\circ$, when imaging a plane with predominantly through-plane flow such as the short-axis plane. However, if through-plane flow is limited, as may occur for patients with low ejection fraction or low heart rates or four-chamber and three-chamber imaging planes, then the FA should be limited to $\sim 75^\circ$.

The second objective was to develop a low SAR 2D breath-hold, cardiac cine imaging technique with blood-myocardium contrast similar to conventional bSSFP imaging using VFA scheme, which was implemented by using an asynchronous k-space acquisition. Bloch simulations were performed to determine if multiple VFA acquisitions of stationary myocardium and flowing blood produces a steady state signal between acquisitions and was verified by phantom experiments. In vivo experiments were also performed in ten healthy subjects with several VFA-bSSFP schemes, and were compared to the conventional segmented bSSFP acquisitions. The novel asynchronous VFA-bSSFP technique can lower the SAR by at least 36% with similar blood-myocardium CNR compared to the conventional bSSFP cardiac cine

imaging. Asynchronous VFA-bSSFP can also be used to increase the CNR by at least 28%, with similar SAR compared to conventional bSSFP.

The third objective was to apply the asynchronous VFA-bSSFP cardiac cine imaging technique for low SAR, 2D free-breathing, bellows gated acquisitions at 3T. Bloch simulations of stationary myocardium and flowing blood were performed to determine the optimal VFA scheme that maximizes the SAR reduction while maintaining blood-myocardium contrast similar to conventional bSSFP imaging. In vivo experiments were performed in ten healthy subjects in both short-axis and long-axis view and the image quality of the bellows gated cardiac cine images (FB-VFA) were compared to standard breath-hold imaging (BH-CFA) using both quantitative metrics and evaluation by two radiological experts. The SAR was reduced by 25% in FB-VFA compared to BH-CFA with similar blood-myocardium contrast and with image quality sufficient to perform global and regional cardiac function analysis.

The fourth objective was to develop a fast, 3D T_2 weighted VFA-bSSFP technique (3D T_2 -TIDE) for prostate imaging at 3T. Conventional 3D fast spin echo techniques take longer acquisition duration for T_2 weighted imaging due to the long recovery time between multi-shot acquisitions. This was overcome in 3D T_2 -TIDE imaging by: 1) designing a VFA scheme for lowering the SAR and hence improving the signal for imaging at 3T; 2) using the transient bSSFP signal for T_2 weighted imaging; and 3) modifying the acquisition of the 3D k_y - k_z plane using spiral-out phase encode ordering for efficient and faster filling of the 3D k-space. Bloch simulations were performed to evaluate the T_2 weighting, contrast between normal prostate tissue and tumor, and the point-spread function of the 3D T_2 -TIDE sequence. In vivo experiments were performed in ten healthy subjects. 3D T_2 -TIDE images were acquired in 2:54 minutes compared to 7:02 minutes for 3D FSE with identical imaging parameters with SNR efficiency that exceeds 3D FSE.

The fifth objective was to develop a VFA scheme to maintain constant transverse magnetization of bSSFP without RF phase alternation ($VUSE_{noalt}$). This novel $VUSE_{noalt}$

sequence has high SNR transient signal but is very off-resonance sensitive. This property of $VUSE_{noalt}$ sequence is used to differentiate the arterial and the venous blood vessels due to their inherent off-resonance differences and was evaluated for non-contrast enhanced MR arteriography of the lower leg. The VFA scheme of $VUSE_{noalt}$ was determined using Bloch simulations and their off-resonance effects were evaluated. In vivo imaging experiments were performed in three healthy subjects and the SNR of arterial and venous blood was compared between $VUSE_{noalt}$, $VUSE$ and conventional bSSFP. $VUSE_{noalt}$ reduces the venous blood signal by a factor of ~ 3 compared to the arterial blood with reduced fat signal.

Overall, VFA bSSFP techniques can be used to lower the SAR or improve the signal for 2D free-breathing cardiac cine imaging, 3D T_2 weighted prostate imaging, and non-contrast MR arteriography of the lower leg.

The dissertation of Subashini Srinivasan is approved.

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1. **Srinivasan S**, Wu HH, Sung K, Margolis DJA, and Ennis DB, Fast Three-Dimensional T2-weighted Imaging with Transition Into Driven Equilibrium balanced SSFP at 3T (*in review*)
2. **Srinivasan S**, and Ennis DB, Optimal Flip Angle for High Contrast Balanced SSFP Cardiac Cine Imaging, Magnetic Resonance in Medicine, 2014; doi: 10.1002/mrm.25228 (*print*)
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THESIS MOTIVATION

Cardiac imaging in conscious pediatric patients is challenging due to the requirement for multiple reproducible breath-held acquisitions. Cardiac cine imaging is routinely performed using balanced steady state free precession (bSSFP) due to the high signal-to-noise ratio (SNR) efficiency and the T_2/T_1 weighted signal that produces bright blood signal and relatively dark myocardial signal. However, bSSFP techniques require the use of: 1) a short repetition time (TR) to reduce the off-resonance induced image artifacts; and 2) a high flip angle (FA) to increase the SNR and CNR. These two requirements increase the deposited RF energy and limit the application of bSSFP especially at high field strengths ($\geq 3T$). The RF energy deposited per unit mass of the object, measured in Watts per kilogram (W/kg) is defined as the specific absorption rate (SAR).

Free-breathing cardiac cine acquisitions can be used to reduce image artifacts due to inconsistent breath-holds or poor breath holding and can reduce patient discomfort. Free-breathing cardiac cine acquisitions, however, have a longer acquisition duration compared to breath-hold acquisitions resulting in prolonged RF energy deposition.

Increased SAR also poses the highest risk for RF induced lead-tip heating and potential tissue damage, which can inhibit pacing and/or ICD shocks for patient with implanted pacemakers or ICDs. Hence low SAR, free-breathing cardiac cine imaging techniques are an important strategy to improve safety and reduce patient discomfort.

T_2 weighted spin echo imaging also requires the use of high flip angles for improved image quality and sufficient contrast. However, this limits the speed of the 3D prostate anatomic imaging at 3T and increases the acquisition duration. The conventional 3D fast spin echo T_2 weighted acquisitions take ~7 minutes to acquire anatomic prostate imaging which increases patient discomfort as well as increases motion sensitivity.

The results described in this dissertation enable low SAR or improved contrast bSSFP applications for free-breathing cardiac cine imaging, fast, 3D T_2 weighted prostate imaging, and non-contrast enhanced MR arteriography of the lower leg.

The **objectives** of this dissertation were to: 1) determine the optimal flip angle for high contrast cardiac cine imaging (Chapter 4); 2) develop a low SAR or high contrast bSSFP cardiac cine imaging technique (Chapter 6); 3) develop free-breathing, low SAR or high contrast bSSFP cardiac cine imaging at 3T (Chapter 7); 4) develop a fast 3D T_2 weighted bSSFP prostate imaging technique at 3T (Chapter 8); and 5) develop ultra low SAR non-contrast enhanced bSSFP MR arteriography of the lower leg (Chapter 9).

OBJECTIVE #1 – Define the optimal flip angle for high contrast bSSFP cardiac cine imaging.

Cardiac cine imaging with bSSFP provides excellent blood-myocardium contrast that depends on the T_1 and T_2 characteristics of the blood and myocardium as well as the imaging flip angle. Conventional Bloch simulations of stationary myocardium and stationary blood have previously established that the optimal flip angle for high blood-myocardium contrast is 54° , but this result was inconsistent with empirical results obtained in vivo. We **hypothesized** that determining the optimal flip angle for high blood-myocardium contrast requires consideration of an imperfect slice profile, flowing blood, and off-resonance. This hypothesis was tested using Bloch simulations, in vivo imaging of healthy subjects as well as clinical patients with a range of cardiac function as explained in Chapter 4.

OBJECTIVE #2 – Develop and evaluate low SAR or high contrast bSSFP cardiac cine imaging.

The bSSFP cardiac cine imaging technique requires using a high flip angle for optimal blood myocardium contrast and hence, increases the SAR and patient discomfort. We **hypothesized** that a variable flip angle (VFA) scheme can reduce the SAR, while maintaining the blood-myocardium contrast as well as image sharpness. Similarly, VFA scheme can also maintain the SAR and improve the blood-myocardium contrast. VFA-bSSFP cardiac cine imaging was performed using an asynchronous cardiac cine acquisition as explained in Chapter 6 and as has

been carefully evaluated with Bloch simulations, phantom experiments, and in vivo imaging in healthy subjects.

OBJECTIVE #3 – Develop and evaluate free-breathing low SAR bSSFP cardiac cine imaging at 3T. Cardiac cine imaging at 3T is SAR limited when using a flip angle greater than about 38° and accords with sub-optimal blood-myocardium contrast. Furthermore, breath-hold cardiac cine imaging can be especially problematic in pediatric patients with or without respiratory impairment. Hence, we ***hypothesized*** that the VFA bSSFP approach can be used to reduce the SAR maintaining the blood-myocardium contrast with bellows gated acquisition to retrospectively reconstruct respiratory motion compensated bSSFP cardiac cine images. The optimal VFA-bSSFP flip angle was determined using Bloch simulations and were validated in healthy subjects as described in Chapter 7.

OBJECTIVE #4 – Develop and evaluate fast 3D T_2 weighted transition into driven equilibrium (3D T_2 -TIDE) bSSFP prostate imaging at 3T. T_2 weighted anatomic prostate imaging is performed clinically using spin echo acquisitions, which are: 1) SAR limited at 3T due to the use of 180° refocusing pulses and; 2) slow due to the fast signal decay and the long delay time required for magnetization recovery. The transient bSSFP signal can be manipulated to produce a T_2 weighted signal, which can be increased using VFA-bSSFP. Consequently, 3D images can be acquired faster using a spiral-out phase encode ordering in k_y - k_z Cartesian plane for efficient sampling. Hence, we ***hypothesized*** that 3D T_2 weighted images can be acquired faster than the conventional spin echo techniques using transient VFA-bSSFP and is described in Chapter 8 using Bloch simulations, and prostate imaging of healthy subjects.

OBJECTIVE #5 – Develop low SAR bSSFP non-contrast enhanced MR arteriography of the lower leg. The bSSFP variable flip angle scheme can be designed to produce constant transverse magnetization to improve the image sharpness as well as to reduce the bSSFP preparation duration. Similarly, the VFA scheme can also be derived for bSSFP without RF phase alternation, which creates constant transverse magnetization with high transient signal

and increased sensitivity to off-resonance. We ***hypothesized*** that this unique property can be used for non-contrast enhanced MR arteriography of the lower leg and is described in Chapter 9 with Bloch simulations, and in vivo lower leg arteriography of healthy subjects.

Collectively, these objectives have enabled the use of variable flip angle techniques for lower SAR, higher contrast, or faster bSSFP applications at 3T for cardiac cine imaging, 3D T_2 weighted prostate imaging and non-contrast enhanced MR arteriography of the lower leg.

Helping to define the context for the chapters reporting on original research are several chapters that provide introductory and background material relevant to each project. Chapter 1 describes the basics of Nuclear Magnetic Resonance, Magnetic Resonance Imaging, and the basics of spin echo and gradient echo imaging. Chapter 2 introduces basics of steady state free precession imaging and the characteristics of bSSFP such as off-resonance and flow effects, catalyzation and transient signals. Chapter 3 introduces cardiac imaging including the acquisition of different cardiac imaging planes and cardiac and respiratory motion compensation. Chapter 5 describes five different variable flip angle techniques that have motivated the other specific aims of this thesis. Chapters 4, 6 to 9 describe the objectives of this thesis in detail. Chapter 10 concludes the thesis and provides an outlook on future work related to these objectives.

CHAPTER 1

INTRODUCTION TO MAGNETIC RESONANCE IMAGING

Magnetic Resonance Imaging (MRI) is a non-invasive medical imaging technique that provides excellent soft-tissue contrast of organs and structures within the body based on the magnetic properties of hydrogen nuclei in the tissue. Compared to the other medical imaging techniques like X-ray, Computed Tomography (CT), Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT) imaging which emit ionizing radiation (100 eV to 100 keV for X-rays; 500 keV for PET imaging), the MR signal is non-ionizing and is in the radiofrequency (RF) range of 10^{-6} eV to 10^{-8} eV.

1.1 Nuclear Magnetic Resonance

When an isotope has an odd number of protons and/or neutrons, such as ^1H , ^{13}C , ^{31}P , they possess an inherent angular momentum ($\vec{J}$) and due to its charge, acts like a tiny bar magnet with a magnetic moment $\vec{\mu} = \gamma \vec{J}$ where γ is the gyromagnetic ratio of the nuclei. When a large magnetic field B_0 is applied, these tiny bar magnets, preferentially align along the direction of the magnetic field either in spin-up state or spin-down state and the energy difference between the two spin states is known as Zeeman splitting. When this is perturbed by an electro-magnetic RF pulse, a nuclear magnetic resonance (NMR) signal will be generated. The frequency of the RF pulse should be equal to the Larmor frequency (ω_0), which is dependent on both the magnetic field as well as the gyromagnetic ratio of the nuclei. The Larmor frequency is given by

$$\omega_0 = \gamma B_0 \quad [1.1]$$

The RF pulse is applied in the direction perpendicular to B_0 to maximize the NMR signal. MR images of structures within the body are generated from ^1H due to its increased abundance in

the body (60-80% of human tissues is water) as well as its increased relative sensitivity. The gyromagnetic ratio of ^1H is

$$\frac{\gamma}{2\pi} = 42.58 \text{ MHz/Tesla} \quad [1.2]$$

The detected MRI signal is the macroscopic ensemble of the magnetic dipole moment per unit volume referred to as the bulk magnetization $\vec{M}$

$$\vec{M} = \sum_i \vec{\mu}_i \quad [1.3]$$

1.2 Bloch Equations

The time dependent behavior of the magnetization under the influence of a static and/or time dependent magnetic field is expressed using the Bloch equations (1). The temporal change of the bulk magnetization due to the torque that acts on $\vec{M}$ in the magnetic field $\vec{B}$ is given by

$$\frac{d\vec{M}}{dt} = \gamma (\vec{M} \times \vec{B}) \quad [1.4]$$

Here the magnetic field $\vec{B}$ may include the effect of both the static magnetic field, B_0 and a time dependent magnetic field $B(t)$. The Eqn. 1.4 does not include the relaxation effects due to spin-spin relaxation or T_2 relaxation and the spin-lattice relaxation or the T_1 relaxation. Including these effects in Eqn. 1.4 and expanding in Cartesian co-ordinates results in the Bloch equations given by

$$\begin{aligned} \frac{dM_x}{dt} &= \gamma (M_y B_z - M_z B_y) - \frac{1}{T_2} M_x \\ \frac{dM_y}{dt} &= \gamma (M_z B_x - M_x B_z) - \frac{1}{T_2} M_y \\ \frac{dM_z}{dt} &= \gamma (M_x B_y - M_y B_x) - \frac{1}{T_1} (M_z - M_0) \end{aligned} \quad [1.5]$$

1.2.1 Rotating Frame of Reference and Free Precession

The Bloch equations are frequently expressed in the rotating frame of reference, to simplify the description of RF excitation and is related to the laboratory frame of reference using the following transformation:

$$\left[\frac{d\vec{M}}{dt} \right]_{lab} = \left[\frac{d\vec{M}}{dt} \right]_{rot} + (\vec{\omega} \times \vec{M}) \quad [1.6]$$

The Bloch equations can be solved in the presence of the external static magnetic field alone, by transforming the Eqn. 1.5 into the laboratory frame and changing the coordinates to x' , y' , $z'=z$

$$\left[\frac{d\vec{M}}{dt} \right]_{rot} = \gamma (\vec{M} \times \vec{B}_0) - (\vec{\omega}_0 \times \vec{M}) = 0 \quad [1.7]$$

$$\frac{dM_{x'}}{dt} = -\frac{1}{T_2} M_{x'}$$

$$\frac{dM_{y'}}{dt} = -\frac{1}{T_2} M_{y'} \quad [1.8]$$

$$\frac{dM_{z'}}{dt} = -\frac{1}{T_1} (M_{z'} - M_0)$$

The solution to Eqn. 1.8 is given by:

$$M_{x'} = M_{x'0} e^{-t/T_2}$$

$$M_{y'} = M_{y'0} e^{-t/T_2} \quad [1.9]$$

$$M_{z'} = (M_{z'0} - M_0) e^{-t/T_1} + M_0$$

where $M_{x'0}$, $M_{y'0}$ and $M_{z'0}$ are the initial conditions, and M_0 is the spin density or the initial magnetization at thermal equilibrium. Eqn. 1.9 represents the free precession of the magnetization. The magnetization along the z-axis is called as longitudinal magnetization and the magnetization along the x-y plane is called the transverse magnetization. The transverse magnetization, decay due to the spin-spin interactions or T_2 relaxation. At the same time, the

longitudinal magnetization along the main magnetic field, recovers with T_1 relaxation or spin-lattice interactions.

1.3 RF Excitation and Forced Precession

The magnetization along the main magnetic field can be perturbed by a time varying magnetic field $B_1(t)$ applied in the direction perpendicular to the main field. Since $B_1(t)$ is applied for a short duration the T_1 and T_2 relaxation can typically be ignored. Hence, during forced precession Eqn. 1.4 can be expressed as

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times (\vec{B}_0 + \vec{B}_1(t)) \quad [1.10]$$

The time-dependence can be removed by transforming the Eqn. 1.10 into the rotating frame,

$$\left[\frac{d\vec{M}}{dt} \right]_{rot} = \gamma \vec{M} \times \left[\left(\frac{\omega_z}{\gamma} + B_0 \right) \vec{k}' + B_1 \vec{i}' \right] \quad [1.11]$$

Magnetic resonance occurs at $\omega_z + \gamma B_0 = 0$. Hence, ω_z has to be less than 0 and replacing $\omega_z = -\omega > 0$ results in

$$\begin{aligned} \left[\frac{d\vec{M}}{dt} \right]_{rot} &= \gamma (\vec{M} \times \vec{B}_{eff}) \\ \vec{B}_{eff} &= \left[\left(B_0 - \frac{\omega}{\gamma} \right) \vec{k}' + B_1 \vec{i}' \right] \end{aligned} \quad [1.12]$$

This is known as forced precession, as the magnetization is now forced to precess along B_{eff} instead of B_0 , with a precession frequency $\omega_{eff} = \gamma B_{eff}$ due to the applied RF pulse. Fig. 1.1 shows the B_{eff} magnetic field in the rotating frame of reference. If a rectangular RF pulse is applied for a duration of T_{rf} , then the magnetization $\vec{M}$ will rotate through an angle $\alpha = \gamma B_1 T_{rf}$ in the $y'z'$ plane.

When the RF excitation pulse is switched off, the magnetization will decay according to Eqn. 1.9 but with $T_2' \ll T_2$, instead of T_2 decay, due to inhomogeneities. If a receiver coil tuned to the same frequency of ω_0 is placed nearby, a voltage signal called the Free Induction Decay (FID)

can be acquired. If this signal is refocused after time $(t)=TE/2$ using a 180° pulse, a spin echo will occur at $t = TE$ where TE is known as the echo time. An example of FID (blue) and spin echo (brown) signal is shown in Fig. 1.2.

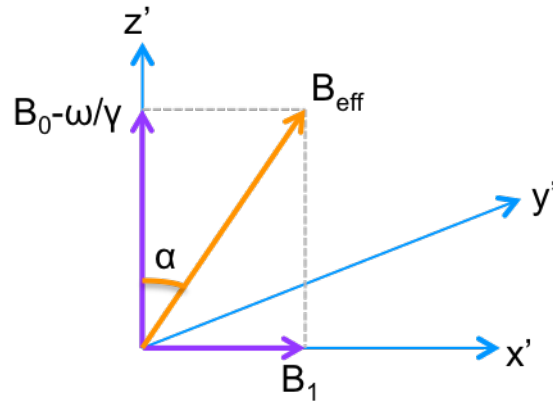


Figure 1.1: If an RF pulse, B_1 , is applied in the x' direction, in the presence of the static magnetic field, B_0 , the magnetization will be forced to precess about the effective field, B_{eff} .

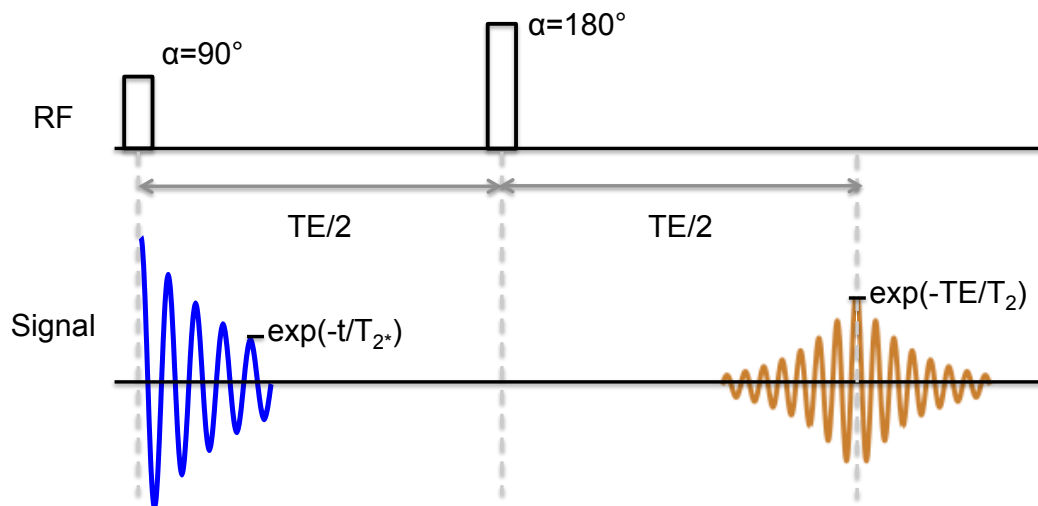


Figure 1.2: The signal after a 90° excitation pulse decays exponentially with time constant T_2^* known as free induction decay. A 180° refocusing pulse at time $(t) = TE/2$

refocuses the signal to generate a spin echo at $t=TE$. The peak magnitude of the spin echo signal is $M_0 \cdot \exp(-TE/T_2)$.

1.4 Spatial Encoding

Both the FID and the echo signal do not have the necessary spatial information to form an image. The spatial information is stored in the MR signal by applying linear magnetic gradients along x-, y- and z-directions. This enables MR images to be acquired in any imaging plane.

1.4.1 Slice Selective Excitation

A two-dimensional slice is selected using a slice-encoding gradient (G_{se}) played in the z-direction, for example, along with the RF excitation pulse (Fig. 1.3a). Because of the slice-encoding gradient along the z direction, only a thin slice of thickness (Δz) is tipped into the x-y plane by the RF excitation pulse of bandwidth ($\Delta\omega$) as shown in Fig. 1.3b. The slice-encoding gradient introduces a linear phase shift across the slice thickness, which needs to be refocused with an opposite gradient along the same gradient axis with half the area of the slice selection gradient. This is called the slice-refocusing (G_{sr}) gradient (2).

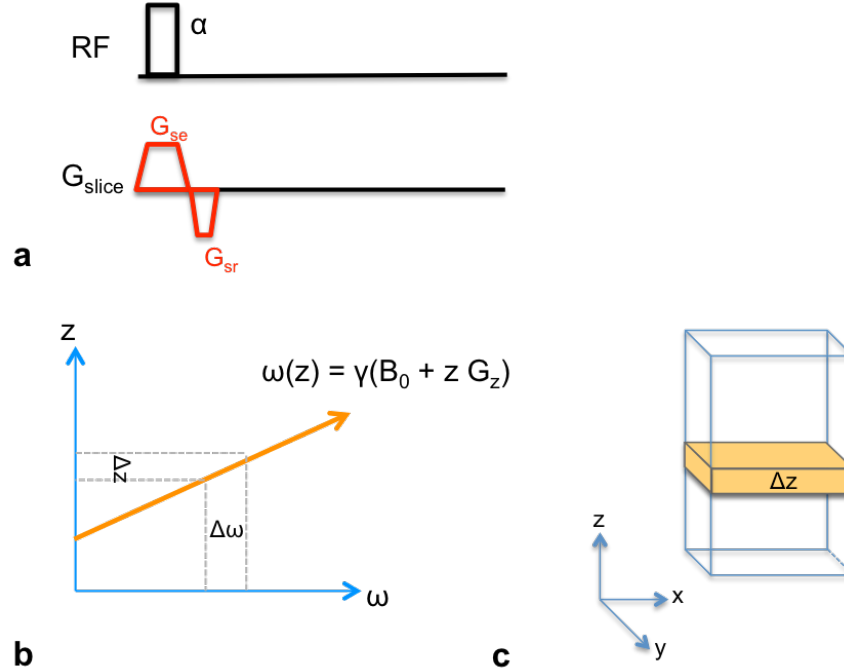


Figure 1.3: The linear slice selective gradient along the z -axis is applied along with the excitation RF pulse (a). A slice of thickness, Δz , is selected by an RF pulse with bandwidth, $\Delta\omega$ (b). The slice thickness can be increased by decreasing the linear z -gradient. Different slices can be selected by changing the frequency, ω , of the RF pulse. The selected slice, Δz , is shown in the image domain in (c).

1.4.2 Phase and Frequency Encoding Gradients

The spatial encoding along the y -axis of the 2D slice is performed using a phase encoding gradient (G_{pe}). This gradient introduces different frequencies $\omega_y = \gamma(B_0 + yG_{pe})$ as a function of y . The spatial encoding in the x -direction is introduced by a frequency encoding gradient (G_{fe}), during read-out, which introduces different frequencies $\omega_x = \gamma(B_0 + xG_{fe})$ along x -axis. The frequency encoding gradient is also referred as the read-out gradient because the analog to digital converter (ADC) of the RF receiver is turned on during the same time. Fig. 1.4 gives a pictorial description of the effect of the phase encoding gradient and the readout gradient on 16 magnetization vectors arranged in a 2D plane. After the RF excitation along the y -axis, at point

1, the signal is along the x-direction. When the phase-encoding gradient is applied along the y-axis, the four rows of magnetization experience increasing phase, along the y-direction shown after point 2 in Fig. 1.4b. The readout gradient introduces linear phase along the x-direction (column), in point 3.

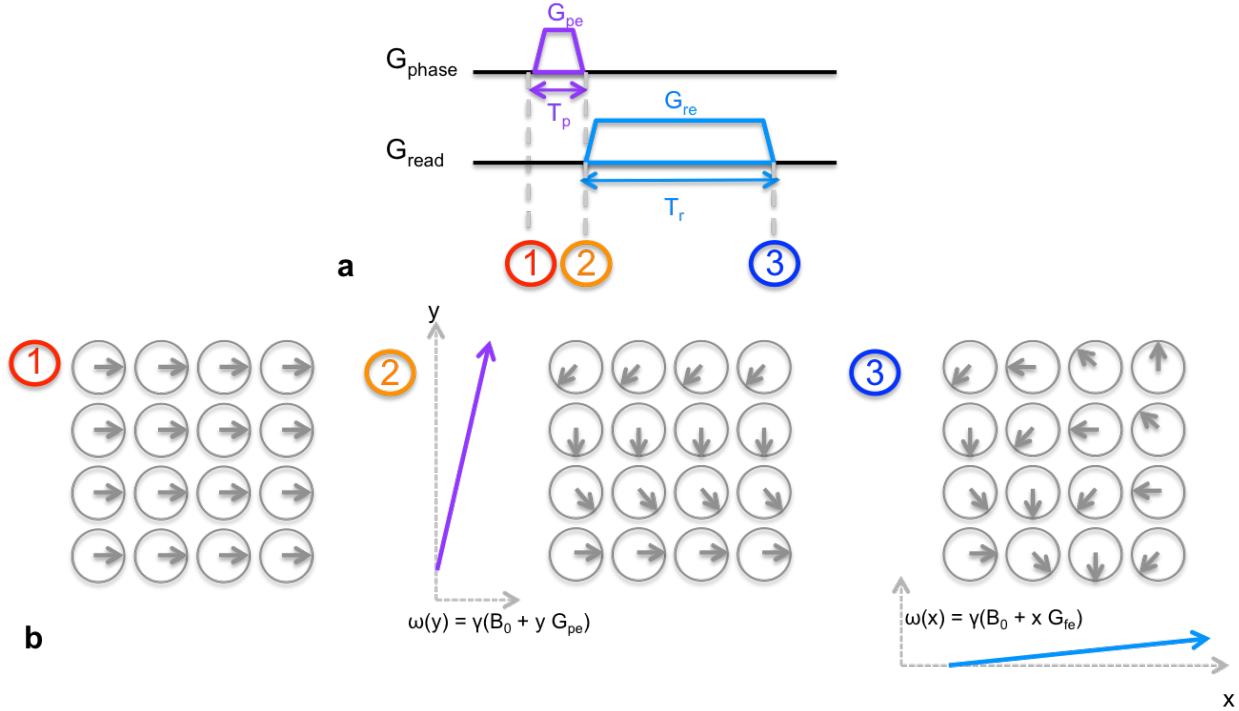


Figure 1.4: The phase introduced by the phase encoding gradient and the readout gradient (a) on a set of 16 magnetization vectors arranged in a 4×4 two-dimensional plane is shown in (b). After the RF excitation, point 1, all the magnetization is aligned in the same direction with phase 0. When the linear gradient is applied along the y-axis, each row experiences a linearly increasing phase, point 2. When the readout gradient is applied, each column experiences an increasing phase, point 3.

The signal (S) of the magnetization at position (x_i, y_j) is proportional to the density of the magnetization (ρ) at that location as well as the phase and frequency due to the phase-encoding and the read-out gradients and is expressed as,

$$S_{ij} \propto \rho(x_i, y_j) e^{i(\omega_{x_i} t + \omega_{y_j} T_p)}$$

$$\omega_{x_i} = \gamma(B_0 + x_i G_{fe})$$

$$\omega_{y_j} = \gamma(B_0 + y_j G_{pe})$$
[1.13]

The readout signal is demodulated at $\omega_0 = \gamma B_0$. The signal acquired in the read-out direction is digitally sampled in $I = [1, 2 \dots N]$ channels at time $t = T_{rl}$. Hence, Eqn. 1.13 can be expressed as

$$S_{ij} \propto \rho(x_i, y_j) e^{i\gamma(x_i G_{fe} T_{rl} + y_j G_{pe} T_p)}$$
[1.14]

1.4.3 k-space

Eqn. 1.14 can be simplified by defining two k-space variables: $k_x = \gamma G_{fe} T_r$ and $k_y = \gamma G_{pe} T_p$. The different points in k_x are acquired continuously for a constant k_y , while the read-out gradient is being played. However, each k_y line is acquired after each TR by varying the phase-encoding gradient. Therefore, the duration to fill the entire k-space is determined by the number of k_y lines and the delay time between the acquisition of adjacent k_y lines. Fig. 1.5 shows an example gradient waveform and the mapping between the gradient space and k-space. In this example, the gradients on each of the axes are played separately to clearly explain the effect of each gradient in the k-space. In practice, the phase-encoding, slice re-phasing, and the read-out pre-phasing gradients are played simultaneously to reduce the acquisition duration as shown in Fig. 1.6.

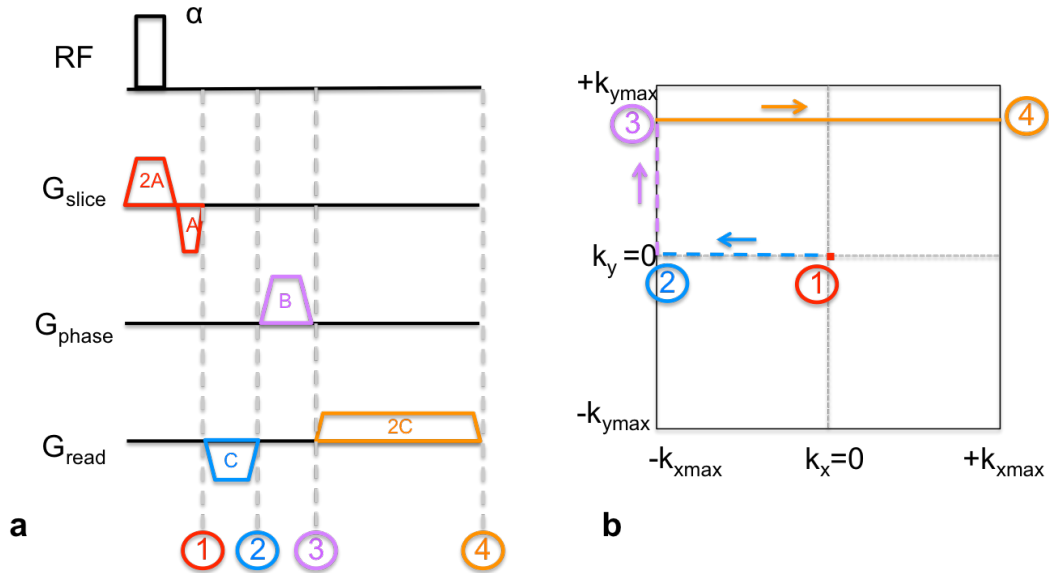


Figure 1.5: An example gradient waveform (a) is used to explain the traversal in k-space (b). A, B and C represent the area within the gradient waveform. At the end of the slice-refocusing gradient, the magnetization will be refocused and will be at the center of the k-space at (1). A negative pre-phasing read-out gradient (blue), will enable traversing from the center of the k-space to $-k_{x\text{max}}$ with constant k_y (2). A positive phase-encoding gradient (purple) will enable traversing from the $(-k_{x\text{max}}, 0)$ towards $+k_{y\text{max}}$ with constant k_x (3). The positive read-out gradient with twice the area of the pre-phasing gradient enables traversal to $+k_{x\text{max}}$ (4).

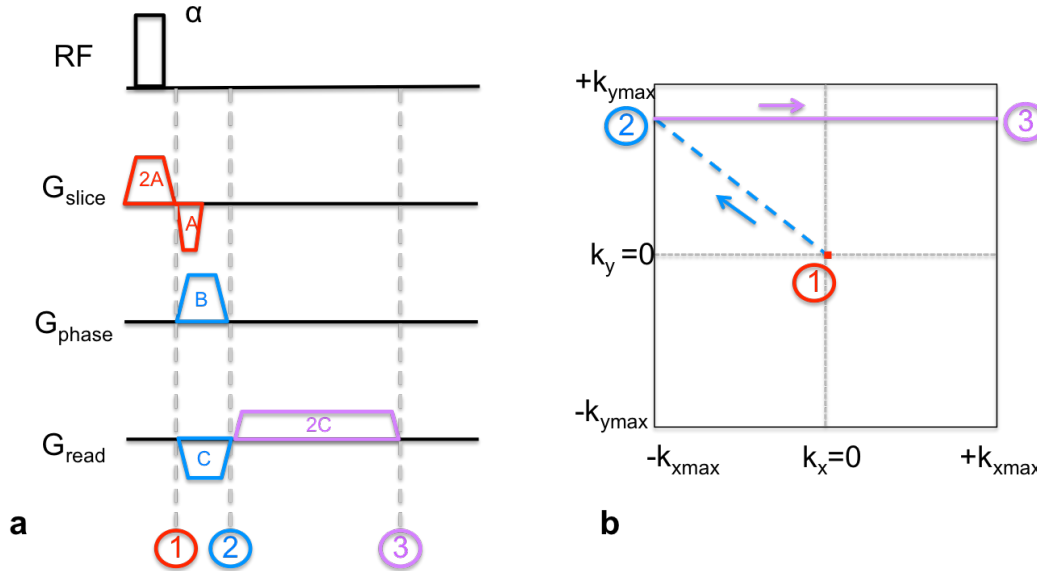


Figure 1.6: An example set of gradient waveforms (a) to k-space (b) mapping explaining the faster traversal in k-space when both phase encoding gradient, B, and pre-phasing gradient, C, along the read-out direction are applied at the same time.

1.5 Image Acquisition

The MRI signal is mainly acquired using spin echo or gradient echo pulse sequences as described below.

1.5.1 Spin Echo Imaging

Fig. 1.7 shows the pulse sequence diagram for two-dimensional spin echo imaging and the mapping from gradient space to k-space. The 90° excitation pulses tips the longitudinal magnetization of the selected slice into the transverse plane. The pre-phasing read-out gradient (G_{rp}) is applied in the x-direction to move from the center of k-space to $-k_{x\text{max}}$. The phase encoding gradient is applied to acquire one k_y line. The 180° refocusing pulse applied at $t=TE/2$, flips the magnetization in the x-y plane and the following readout gradient and the ADC are used to acquire the spin echo at $t=TE$. The duration from the excitation to center of the read-out

gradient is called the echo time (TE). The transverse signal is allowed to decay for some time $t=TR \gg T_2 > T_1$ of the tissue. This time delay is called as repetition time. This is followed by another acquisition with a different phase-encoding gradient to acquire the subsequent k_y line. These steps are repeated until all the k_y lines are acquired. The spin echo signal is given by

$$S_{SE} \propto \rho \left(1 - e^{-\frac{TR}{T_1}} \right) e^{-TE/T_2} \quad [1.15]$$

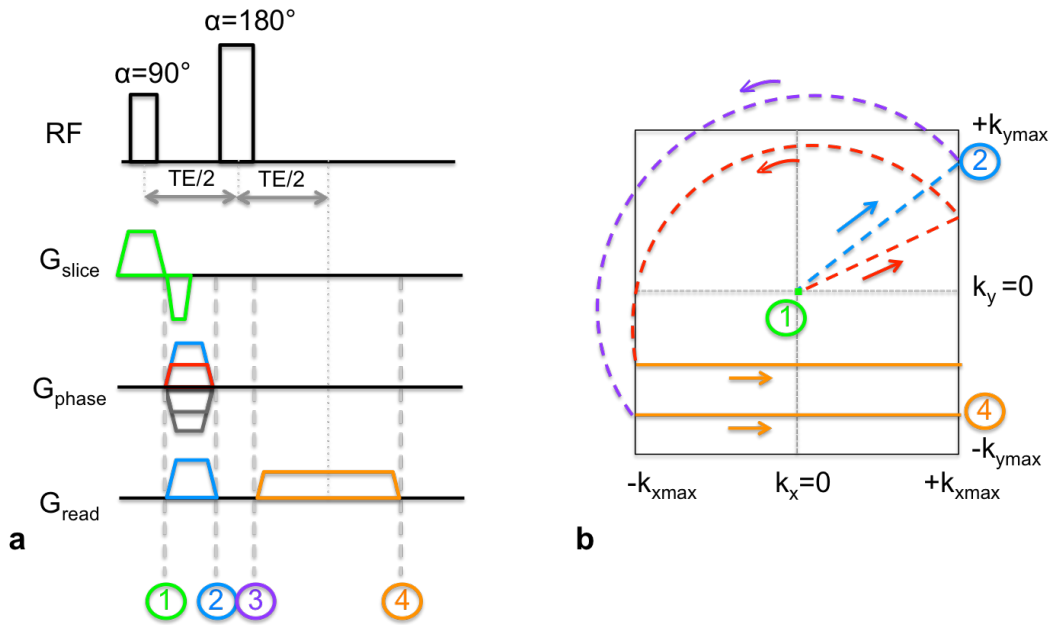


Figure 1.7: Spin echo pulse sequence diagram (a) and the corresponding gradient to k-space mapping (b). The 90° excitation pulse tips the longitudinal magnetization completely into the transverse plane. The phase encoding and pre-phasing readout gradient (blue), traverse towards the top right of the k-space (2). The 180° pulse flips the magnetization towards the bottom left of the k-space (3) and the corresponding k_y line is read-out (4). During the subsequent TR, another phase encoding gradient (red) is applied to acquire a different k_y line.

The spin echo imaging is the most clinically used sequence because the refocusing pulse, refocuses the B_0 inhomogeneities, hence the images do not have off-resonance artifacts unlike other gradient echo based techniques. The image contrast of spin echo imaging can be adjusted by varying the TR and the TE. If the TE is short ($TE \ll T_2$) and $TR \sim T_1$, then the spin echo signal will be T_1 weighted. If the TR is long ($TR \gg T_1$), and $TE \sim T_2$, then T_2 weighted images can be acquired, and if TR is long ($TR \gg T_1$) and TE is short ($TE \ll T_2$), then proton-density weighted images can be acquired.

The 180° refocusing pulse of the spin-echo sequences deposit more energy and are especially problematic at 3T due to the increased energy deposition at higher field-strengths. Variable Flip Angle techniques can be used to lower the RF energy deposition as described in more detail in Chapter 5.

1.5.2 Gradient Echo Imaging

Gradient echo imaging (GRE) uses a gradient to create the signal echo instead of an energy intensive 180° refocusing pulse. The pulse sequence diagram and corresponding k-space of two-dimensional gradient echo imaging is shown in Fig. 1.8. Gradient echo imaging uses a flip angle (α) less than 90° , and results in the tipping of the longitudinal magnetization. Hence, the transverse component of the magnetization will not be M_0 unlike the spin echo sequence, and the magnitude of the GRE signal will be lower than the magnitude of a spin echo signal. It is for this same reason that the signal recovers faster in GRE and the image acquisition duration is reduced compared to spin echo.

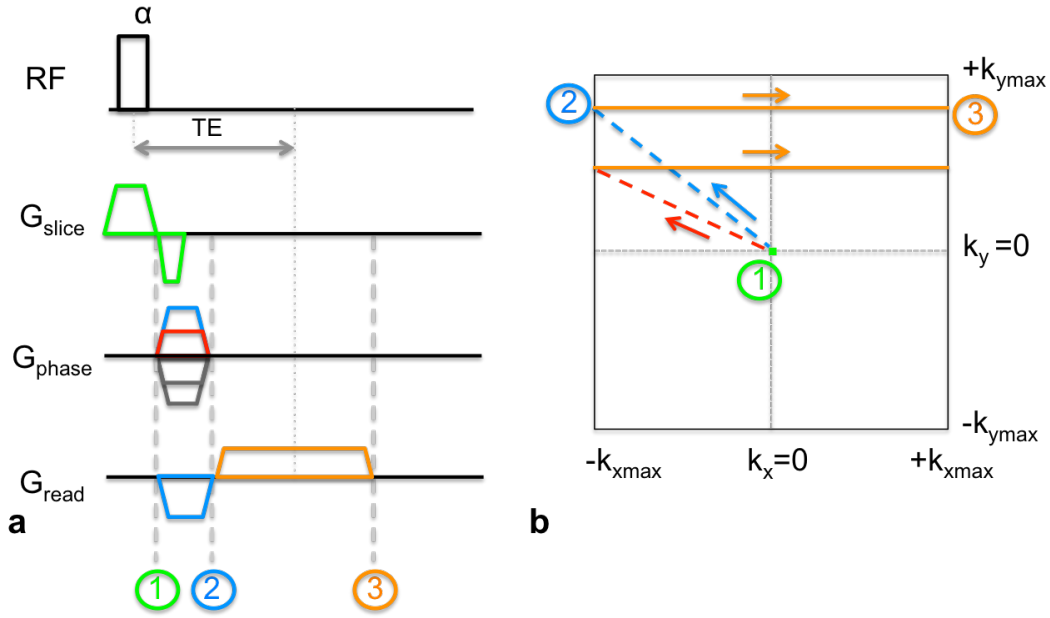


Figure 1.8: Gradient echo pulse sequence diagram (a) and the corresponding k-space diagram (b). The α excitation pulse tips the magnetization towards the transverse plane. The phase encoding and pre-phasing readout gradient (blue), traverse towards the top left of k-space (2) and the corresponding k_y line is read-out (3). During the subsequent TR, another phase encoding gradient (red) with different magnitude, is applied to acquire a different k_y line.

The pre-phasing read-out gradient in GRE is used to dephase the FID signal and the first half of the read-out gradient rephases the signal and forms the gradient echo at $t=TE$. Similar to the spin echo imaging, different k_y lines are acquired by varying the amplitude of the phase encoding gradient. The signal equation of GRE depends on the TR, TE and α of the RF pulse and is given by

$$S_{GRE} \propto \rho \frac{\sin \alpha \left(1 - e^{-\frac{TR}{T_1}} \right)}{\left(1 - \cos \alpha e^{-\frac{TR}{T_1}} \right)} e^{-TE/T_2^*} \quad [1.16]$$

The GRE echo signal is T_2^* weighted instead of T_2 weighting, because of the absence of 180° refocusing pulse. Hence, GRE imaging is clinically used for either T_1 weighted imaging or susceptibility (T_2^*) weighted imaging. The TR of the GRE sequence can be further reduced, by applying a spoiler gradient to spoil the excess transverse magnetization within each pixel/voxel. By applying a phase-rewind gradient before the spoiler will make GRE a faster, steady-state sequence (Chapter 2).

1.5.3 Three Dimensional Imaging

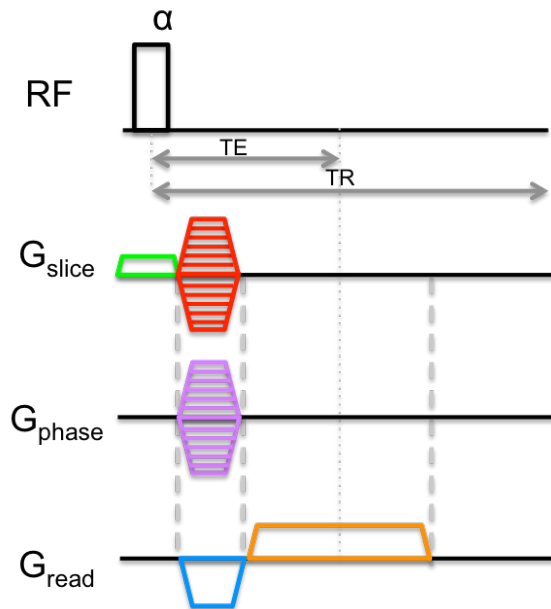


Figure 1.9: Three-dimensional gradient echo pulse sequence diagram. The varying amplitude phase encode gradients are present in both slab and conventional phase-encoding direction to encode z and y directions. The signal has to be acquired $N_z \times N_y$ times to completely fill the 3D k-space where N_z and N_y are the number of phase encoding gradient steps in z and y directions respectively.

Three Dimensional imaging is performed using a slice-selective excitation pulse to excite a three-dimensional slab. Phase encoding will be performed in both the slab and phase encode

directions to spatially encode both the y and z direction followed by the read-out gradient to encode the x-direction as shown in Fig. 1.9.

1.6 Image Reconstruction

The k-space signal is the Fourier transform of the image. Hence, a two-dimensional Fourier transform of the k-space data will result in a 2D image. The complex Fourier transform can be used to reconstruct both absolute magnitude image and the phase image. The magnitude image is used widely for anatomic imaging while the phase is used for quantitative measurements such as measuring velocity in phase contrast imaging and estimating B0 field inhomogeneities in fat-water separation. As each k_y line is acquired after every TR, the image reconstruction can also be performed faster by performing two series of one-dimensional Fourier transforms. The image quality can be quantitatively analyzed by calculating the signal to noise ratio and contrast to noise ratio.

1.6.1 Signal to Noise Ratio

Signal to Noise Ratio (SNR) is the ratio of the mean signal to the standard deviation of the background noise. SNR depends on the voxel volume, number of measurements and the receiver bandwidth (BW) by:

$$SNR \propto (\text{voxel volume}) \sqrt{\text{total sampling time}}$$

$$SNR_{2D} \propto \left(\frac{FOV_x}{N_x} \frac{FOV_y}{N_y} \Delta z \right) \sqrt{\frac{N_x N_y N_{avg}}{BW}} \quad [1.17]$$

$$SNR_{3D} \propto \left(\frac{FOV_x}{N_x} \frac{FOV_y}{N_y} \frac{FOV_z}{N_z} \right) \sqrt{\frac{N_x N_y N_z N_{avg}}{BW}}$$

The field of view (FOV) is the imaging dimension along each of the axes and N_i is the number of pixels that are acquired along each FOV_i . Hence, the pixel dimension for the x-axis and y-axis is

calculated as FOV_x/N_x and FOV_y/N_y respectively. In 2D imaging, the dimension along the z-axis is the slice thickness, Δz . N_{avg} is the number of repetitions that each image is acquired to get an averaged image. A single slice in 3D imaging has an SNR gain of $\sqrt{N_z}$ compared to the same slice acquired in 2D imaging.

Image SNR is typically defined using Region of Interest (ROI) analysis. An ROI is drawn over a specific region and the mean signal of the pixels with the region is determined. The noise is determined by drawing a similar ROI outside the imaging volume in the background. SNR is measured as the ratio of the mean signal to the standard deviation of the background noise. The noise can also be measured more accurately by acquiring images with identical pulse sequence with zero RF signal amplitude (3). The received MR signal can also be increased, by using localized, multi-channel surface coils, for signal reception. The noise in multi-channel acquisitions has a Rayleigh distribution (4) and the standard deviation has to be corrected by a factor of $\sqrt{\frac{2}{4-\pi}} = 1.53$. SNR efficiency is calculated as the ratio of the SNR to the square root of the image acquisition duration.

1.6.2 Contrast to Noise Ratio

Contrast between two different tissue types such as myocardium and blood, myocardium and lung tissue, or normal prostate tissue and prostate tumor tissue is typically maximized to better delineate the structures. Fig. 1.10 shows example cardiac images with poor blood-myocardium contrast and excellent blood-myocardium contrast.

The contrast between different tissues is maximized by maximizing the signal difference between the two tissues (Eqns. 1.15, 1.16, 2.1) and depends on the choice of imaging parameters such as flip angle, TE and TR and the relaxation properties inherent to each tissue.

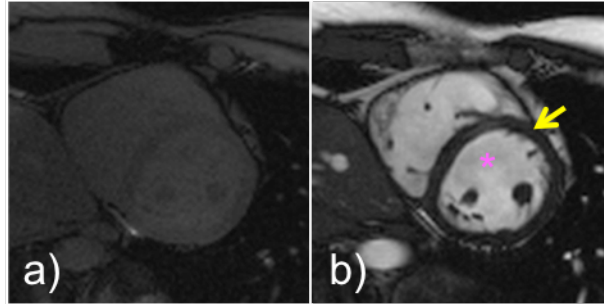


Figure 1.10: Example cardiac images acquired with low flip angle (FA)=15° (a) and high FA=70° (b) shows that the contrast between the blood (magenta star) and myocardium (yellow arrow) can be improved (b) using a higher flip angle.

Image Contrast to Noise Ratio (CNR) is also determined using ROI analysis as the ratio of the difference between mean signal intensity in two different tissues to the standard deviation of the background noise.

1.7 MRI Safety

MRI is generally a safe imaging technique without ionizing radiation. However, precautions need to be taken due to the projectile effects that can arise from the main magnetic field, heating due to the RF field, and the peripheral nerve stimulation due to the rapid switching of the gradient fields.

1.7.1 Projectile risk

The MR magnet is a superconducting magnet and is always on. The strong magnetic field can interact with ferromagnetic objects (e.g. medical device implants) causing translational attraction and/or torque that may cause movement or dislodgement, resulting in injury or dysfunction of the device. Hence, ferromagnetic objects should not be allowed near the scanner and the patients need to be evaluated thoroughly for such objects before entering the scanner room. MRI is also broadly contraindicated for patients with neuro-stimulators, artificial valves,

ferromagnetic surgical implants, surgical clips, tattoos with ferromagnetic particles, cardiac pacemakers and ICDs. Many devices are being manufactured and designated as MRI-Safe or as MRI-Conditional (per FDA guidelines and review). Patients with MRI-Conditional devices should be cautiously scanned using MRI following strict guidelines provided by the manufacturer.

1.7.2 Specific Absorption Rate

The RF pulses deposit RF energy that can cause heating, which is measured by specific absorption rate (SAR) in watts per kilogram weight of the individual. The clinical scanners check the SAR deposited by each pulse sequence and are limited by the FDA (Food and Drug Administration) regulations on the maximal amount of SAR that can be deposited in patient's head, torso, whole body and extremities. In "Normal Level" the maximum head SAR is 3.2 W/kg and whole body is 2 W/kg and in "First Level", the maximum SAR limitation in the head is 3.2 W/kg and for the whole body is 4 W/kg.

SAR is proportional to the square of the magnetic field strength, square of the flip angle, induced electric field, tissue density, conductivity and patient size (2). Hence, at higher field strength, SAR is especially problematic. For example, Fig. 1.11 compares the predicted whole body SAR, predicted head SAR, and the SAR measured during a time interval of 360s and 10s, from both 1.5T (Siemens, Avanto) and 3T (Siemens, Trio) scanners. Identical phantom images were acquired using the head coil with FOV=200×200 mm, acquisition matrix=250×256, TR/TE= 4.3/2.16 ms, BW=930 Hz/px, and averages=15 acquired for a duration of 17.3 seconds for a range of FAs until SAR was limited at 3.2 W/kg for the head scan. Identical imaging parameters were used to acquire images on both scanners. The bore temperature was 23°C in Trio during the scan and was 24°C in Avanto.

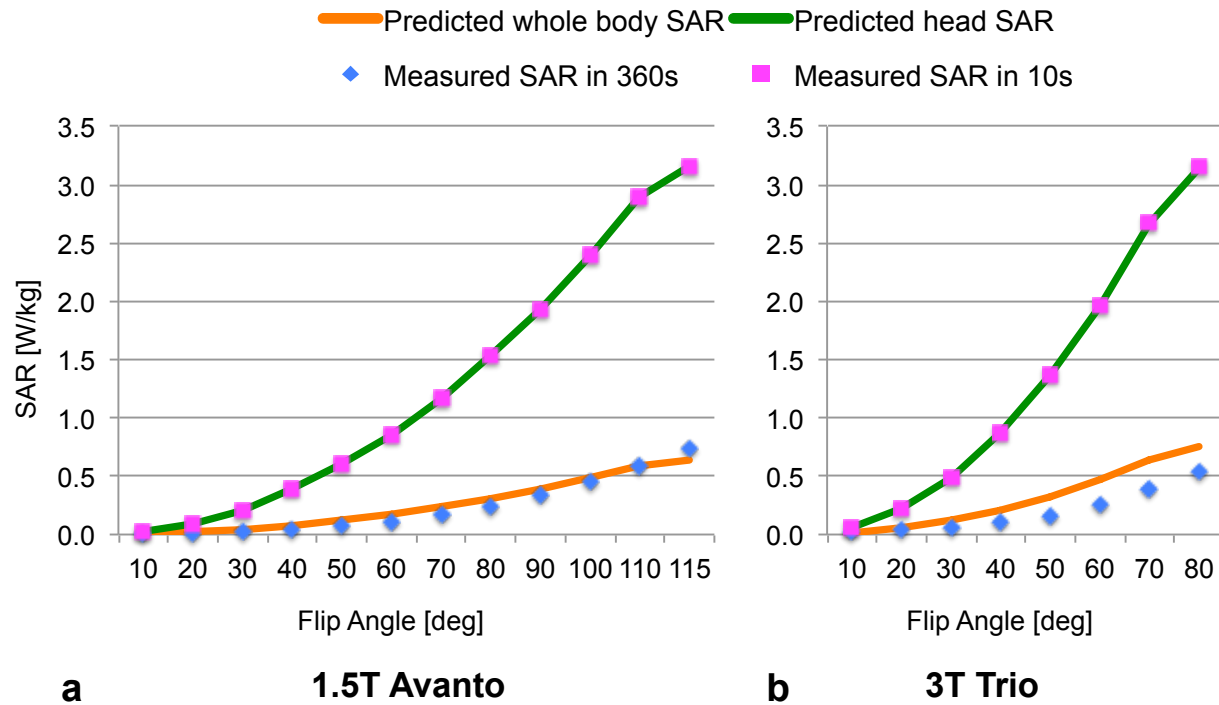


Figure 1.11: Predicted whole body (orange solid line) and head SAR (green solid line) compared to measured SAR during the scan within a time interval of 360s (blue diamonds) and 10s (magenta squares) using both a 1.5T Avanto scanner (a) and a 3T Trio (b) scanner. The predicted head SAR and the measured SAR during 10s increases with increasing flip angle and reaches a maximum SAR limit at 115° flip angle in 1.5 T and 80° flip angle in 3T.

In addition to the predicted whole body SAR and predicted head SAR, the Siemens scanners also predict SAR for eight other different variables. The corresponding limits for the different averaging times for a Bore Temperature of 24°C with a head coil are shown in Table. 1.1. The highest predicted SAR out of these 10 variables, is used to limit the maximum FA that can be used for a pulse sequence. The scanner also measures the energy of measurement for each acquisition, which is reported in units of W•s.

	360 seconds	90 seconds	10 seconds
Whole Body (W/kg)	2 (4)	4 (8)	6 (12)
Exposed Body (W/kg)	7.4*	14.7*	22.1*
Head (W/kg)	3.2	6.4	9.6
Head Local (W/kg)	10	20	30
Torso Local (W/kg)	10	20	30
Legs Local (W/kg)	20	40	60
B1ms (μT^2)	50 (100)	100 (200)	150 (300)
Coils (W)	146.2*,#	-	438.7*,#
BCCable (W)	99999	-	99999
LCCable (W)	99999	-	99999

Table 1.1: Predicted SAR limits for the different variables calculated by the scanner at three different time intervals for a prescribed head scan in 3T at “Normal Level”. The values in parenthesis are the SAR values at “First Level”. * denotes that the SAR is dependent on the patient mass. # denotes that the field strength dependent SAR limit.

Variable flip angle imaging can be used to lower the SAR of spin echo and steady-state imaging techniques and is detailed in Chapter 5. SAR is also a concern while imaging patients with implanted devices like pacemaker or ICDs (5). The RF induced E-field can inductively couple with the conductive electronics of the implant and resistive heating can occur where there are substantial current paths. This can lead to significant heating, for example, near the lead-tip of both pacemakers and ICDs, which can damage tissue (6).

1.7.3 Gradient Slew Rate

The linear gradients along the x, y and z directions are switched rapidly during, for example, spatial encoding. This rapid switching of gradients produces noise and hence MRI scans are noisy and individuals need to be provided with earplugs before a MRI scan. The rapid switching of the gradients can also cause peripheral nerve stimulation (7) and hence, the slew rate of the gradient should not exceed a threshold value (e.g a maximum slew rate of $200 \text{ Tm}^{-1}\text{s}^{-1}$) set by the MRI scanner manufacturers based on volunteer studies.

CHAPTER 2

STEADY STATE IMAGING

The conventional gradient echo and spin echo imaging techniques require a long TR for the complete decay of the transverse signal, which also results in longer image acquisition times. Steady state imaging refers to acquiring signals with short $TR \ll T_2 < T_1$. In this imaging technique, the transverse signal does not completely decay before the acquisition of the subsequent signal and hence, the signal can be both T_1 and T_2 weighted. Both the transverse and the longitudinal signal reach steady state if the pulse sequence satisfies the following four conditions (8):

1. The TR has to be constant
2. The dephasing due to the gradients is constant along the slice, phase encoding and read out direction for every TR: $\int G(t)dt = c$
3. The flip angle is constant
4. The phase of the RF pulse must satisfy the equation: $\Phi_n = a + bn + cn^2$

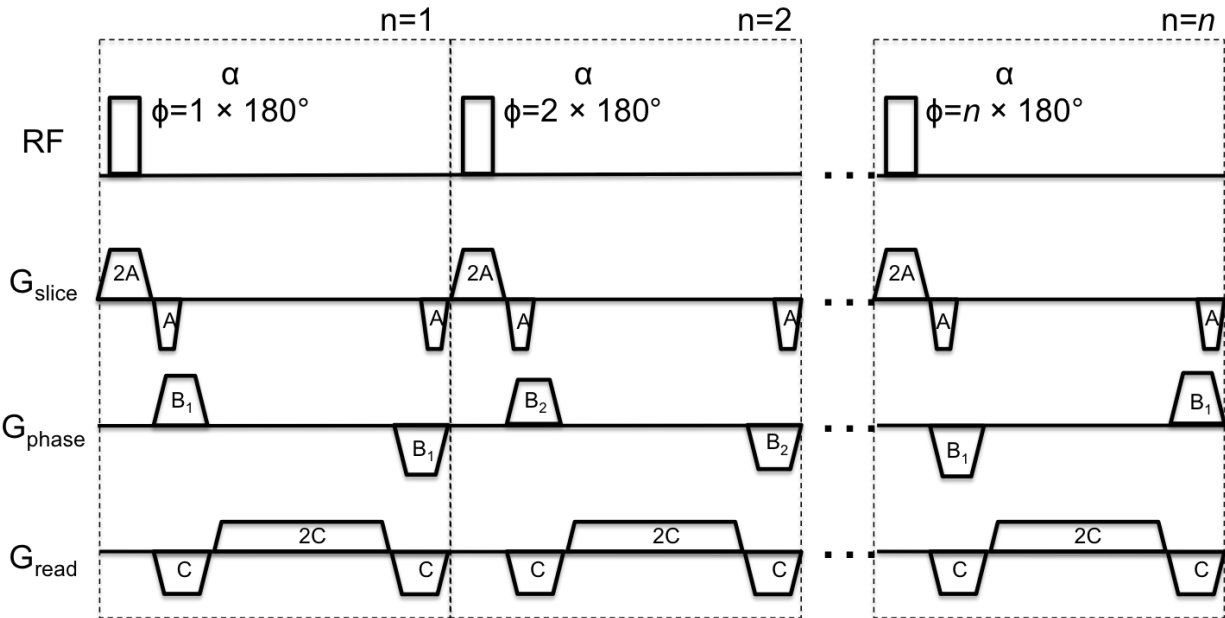


Figure 2.1: Pulse sequence diagram for the balanced steady state free precession sequence with dotted rectangle representing each TR. The phase of the RF pulse is

alternating every TR between 180° and 0° . A, B_i and C represent the gradient area in the slice, phase and read-out axis. The sum of the gradient along each axis for each TR is constant and is equal to zero.

Fig. 2.1 shows an example steady state sequence with constant gradient dephasing equal to zero. The phase of the odd RF pulses is 180° and the phase for even RF pulses is 0° . Since the gradient area along the slice select, read, and phase encoding direction is equal to zero and the RF pulse's phase alternates between each TR, this sequence is completely balanced and is referred as balanced Steady State Free Precession technique (bSSFP).

2.1 Signal Characteristics of bSSFP

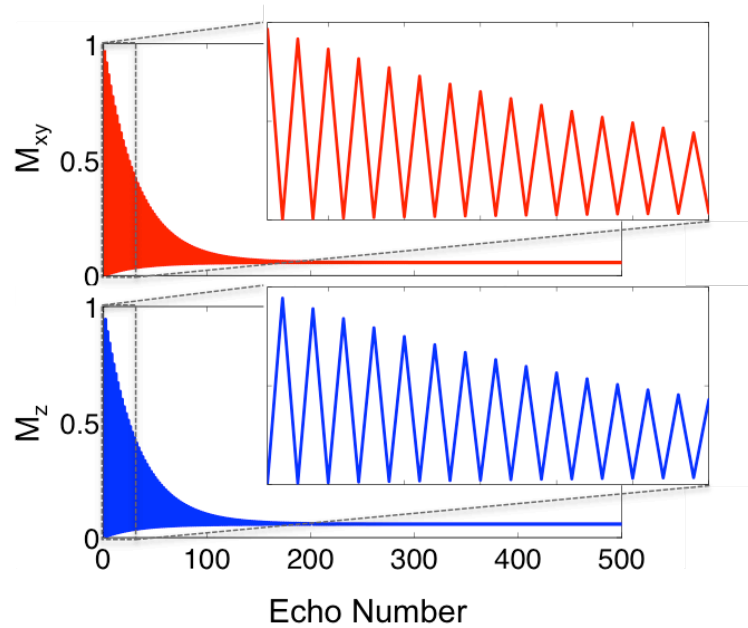


Figure 2.2: Simulation of the transverse magnetization (M_{xy}) and longitudinal magnetization M_z with echo number for on-resonant spins. The transient signal (zoomed) oscillates wildly before reaching steady state after ~200 echoes.

Fig. 2.2 shows a simulated on-resonant transverse and longitudinal magnetization with respect to the number of echoes for a tissue with $T_1/T_2=1000/60$ ms, FA (α) = 90° , $M_0=1$, $TR=3.5$ ms and $TE=TR/2$. Both the transverse and longitudinal magnetization oscillate wildly before reaching a steady-state signal. The steady state transverse signal for bSSFP is given by,

$$bSSFP_{ss} = M_0 \sin \alpha \frac{1 - E_1}{1 - (E_1 - E_2)\cos\alpha - E_1 E_2} e^{-TE/T_2} \quad [2.1]$$

where $E_{1,2}=\exp(-TR/T_{1,2})$. When $TR \ll T_2 < T_1$

$$bSSFP_{ss} \simeq M_0 \sin \alpha \frac{1}{(T_1/T_2)(1 - \cos\alpha) + (1 + \cos\alpha)} e^{-TE/T_2} \quad [2.2]$$

Note the T_2/T_1 weighting factor in the denominator of the steady state signal in Eqn. 2.2. Hence, bSSFP contrast is T_2/T_1 weighted. The bSSFP signal is completely refocused in every TR by the balanced gradients and results in a refocused signal at $TE=TR/2$ similar to a spin echo sequence. Hence the steady state signal in Eqn. 2.2 is weighted by $\exp(-TE/T_2)$ unlike the gradient echo sequences which are weighted by a factor of $\exp(-TE/T_2^*)$ (9). The optimal flip angle for maximum on-resonant, stationary tissue bSSFP signal can be derived from Eqn. 2.2 and results in the following optimal flip angle and signal:

$$\alpha_{opt} = \arccos\left(\frac{E_1 - E_2}{1 - E_1 E_2}\right) \quad [2.3]$$

$$bSSFP_{ss, \alpha_{opt}} \simeq \frac{M_0}{2} \sqrt{\frac{T_2}{T_1}} \quad [2.4]$$

Fig. 2.3 shows the dependence of the bSSFP steady state on the FA and T_2/T_1 ratio. The highest steady state signal of $0.5M_0$ is reached only for a tissue with T_2/T_1 ratio of one and a FA of 90° . This is the maximum steady state signal achievable with a short TR for any MRI sequence. Hence, bSSFP has high SNR efficiency. Both the optimal FA and the steady state signal decrease with decreasing ratio of T_2/T_1 . The optimal FA for bSSFP sequences is higher than the optimal FA used in other steady-state sequences.

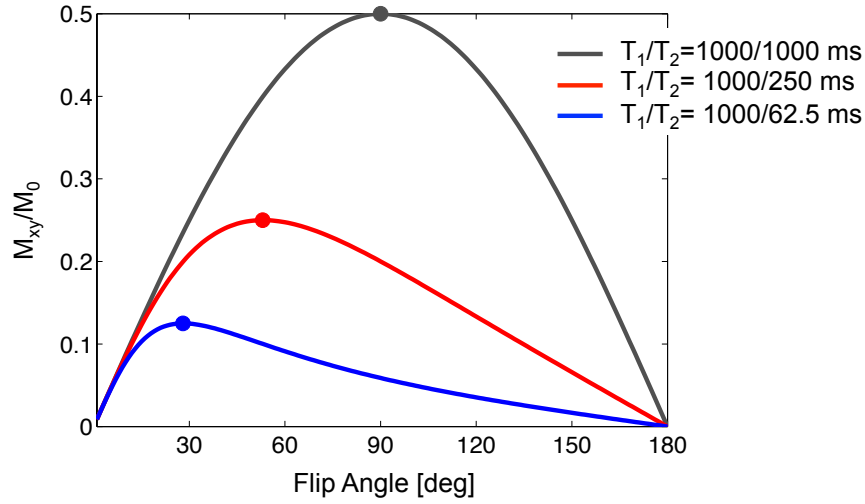


Figure 2.3: Simulation of the bSSFP steady state signal for FA ranging from 1° to 180° for three different tissues with T_1/T_2 ratio of 1 (gray), 4 (red) and 16 (blue). The optimal FA for high signal is shown in circles. The maximum steady state signal and the optimal FA decrease with increasing T_1/T_2 ratio.

2.2 Off-resonance effects

The bSSFP signal is strongly dependent on the dephasing due to off-resonance or B_0 inhomogeneities. Fig. 2.4a shows the steady state signal simulation with respect to different off-resonances for a tissue with T_2/T_1 ratio of one and $TR=3.5$ ms. The steady state signal is close to zero when the off-resonance is $\pm 180^\circ$. This characteristic of bSSFP results in banding artifacts in the images at the locations with off-resonance close to multiples of $\pm 180^\circ$. The dephasing angle in radians within a TR can be expressed as $\theta=2\pi \cdot v \cdot TR$ where v is the frequency offset between the RF synthesizer and local precession frequency (10). A dephasing angle of $\pm 180^\circ$ occurs at $v=\pm 1/(2 \cdot TR)$. Hence, bSSFP images are acquired with the shortest possible TR to increase the width of the pass-band (distance between two adjacent bands) and reduce the banding artifacts within the region of interest in the field of view. However, the combination of a short TR and a high optimal FA, makes bSSFP sequences SAR intensive. The

B_0 inhomogeneities also increase with increasing field strength making bSSFP imaging challenging at higher field strengths ($\geq 3T$).

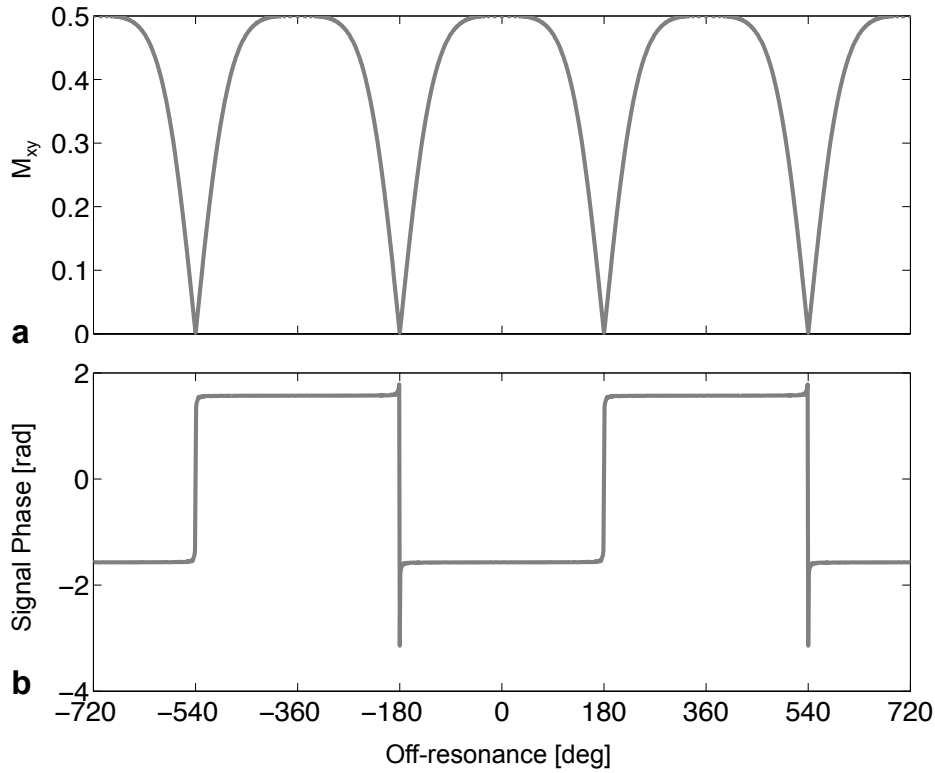


Figure 2.4: Simulation of the absolute steady state signal (a) and phase of the signal (b) with different off-resonance ranging from -720° to 720° .

The corresponding phase of the steady state signal (Fig. 2.4b) shows that the phase is constant within adjacent multiples of 180° and alternates in the next adjacent frequency intervals. Say for example, the phase is constant and negative within $\pm 180^\circ$ (Fig. 2.4b) and flips to a positive phase between 180° and 540° . This property of bSSFP, with appropriate choice of TR, is used for fat water separation of cardiac cine images (11) as well as peripheral angiography (12).

The opposing phase of the bSSFP signal results in the “india-ink artifact” at the fat-water interfaces (13). This occurs when the fat signal and the water signal have opposite phases at a

particular TR and field strength and causes destructive interference at the fat-water interface due to partial volume effects. The india-ink artifact can be reduced by adjusting the TR such that the phase of the fat and phase of the water are equal. Note that bSSFP imaging is predominantly acquired with $TE=TR/2$. However, if $TE \neq TR/2$, the effect of the phase at the TE has to be considered.

2.3 Frequency Scout Imaging

The B_0 inhomogeneities increase with increasing field strength and are especially higher within the field-of-views used for cardiac imaging adjacent to the heart-lung interface. The bSSFP banding artifacts can be shifted within the field-of-view by varying the frequency of the RF pulse. This property of bSSFP is especially used during cardiac cine imaging at 3T where multiple images of the heart are acquired by varying the frequency of the RF pulse (14). The frequency shift that shifts the banding artifacts outside the imaging region or the image with the least artifact within the heart is chosen for subsequent cardiac cine imaging.

2.4 Catalyzation of bSSFP

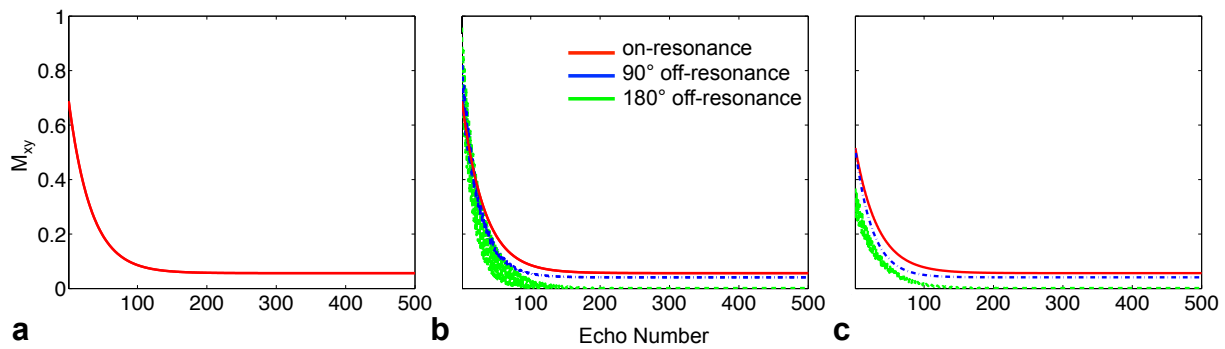


Figure 2.5: Simulation of the transverse magnetization (M_{xy}) with echo number for a tissue with $T_1/T_2=1000/60$ ms, $\alpha = 90^\circ$, $M_0=1$, $TR=3.5$ ms and $TE=TR/2$. (a) $\alpha/2$ pulse with a delay of $TR/2$ reduces the signal oscillations compared to Fig. 2.2 but the off-resonant spins still have signal oscillations (b) which are comparatively reduced (blue

and green) using 30 Kaiser Bessel pulses (c). Kaiser Bessel pulses also enable faster transition to steady state signal.

The transverse magnetization of the bSSFP signal oscillates (Fig. 2.2) for a duration of about $5 \times T_1/TR$ (15) before reaching steady state. During this period, acquisition of the signal will result in image artifacts. Several techniques have been proposed to reduce the signal oscillations during the transient state of bSSFP. The simplest and most commonly used preparation pulse is a $\alpha/2$ pulse with a delay of $TR/2$ followed by bSSFP imaging acquisition. This preparation reduces the signal oscillations during the transient state (Fig. 2.5a). However, this preparation pulse does not reduce the oscillation for off-resonant magnetization (Fig. 2.5b). Alternatively, linear ramp (16,17) or Kaiser Bessel (18) ramp pulses are used to reduce the oscillation of both on-resonance and off-resonant magnetization as well as reduce the duration to reach steady-state. Fig. 2.5c shows the signal simulation with 30 Kaiser Bessel pulses.

2.5 Transient bSSFP Signal

The on-resonant bSSFP transient signal (15) in Fig. 2.5a can be expressed as

$$M(n) = \left(\sin\left(\frac{\alpha}{2}\right) M_0 - M_{ss} \right) \lambda^n + M_{ss} \quad [2.5]$$

where n is the echo number, M_{ss} is the steady state signal in Eqn. 2.1 and λ is the decay rate of the transient signal and is given by

$$\lambda \simeq E_2 \sin^2\left(\frac{\alpha}{2}\right) + E_1 \cos^2\left(\frac{\alpha}{2}\right) \quad [2.6]$$

When bSSFP images are acquired during the transient state with a flip angle of 180° , the steady state signal approaches 0 and $\lambda \simeq E_2$ and is purely T_2 weighted similar to spin echo imaging. Since, the signal is completely refocused with 180° pulses, the images will not have off-resonance artifacts. However, RF pulse with imperfect slice profiles cannot eliminate the off-

resonance artifacts. This property of bSSFP imaging has been reported for T_2 weighted edema imaging of the heart (19).

2.6 Flow effects in bSSFP

The first moment of the readout and the slice encoding direction is zero and hence the bSSFP sequence is flow compensated along both of these axes. However, the phase encoding gradient is not first moment compensated, which results in flow artifacts in the bSSFP sequence especially for cardiac segmented sequences (See chapter 3.3). These artifacts can be reduced in segmented cardiac sequences using paired phase-encoding k-space acquisitions (20), which is also used for reducing eddy current artifacts in cardiac imaging (21).

However, the first moment compensation in bSSFP sequences also demonstrates flow artifacts. In the spoiled GRE sequences, the flow signal decays faster due to T_2^* decay in combination with the application of the spoiler gradients at the end of TR. But, in the presence of fully compensated bSSFP gradients, the T_2^* decay takes a longer time and still contribute to the measured signal resulting in slice broadening for the flow signal (22,23).

CHAPTER 3

CARDIOVASCULAR MAGNETIC RESONANCE IMAGING

Cardiac magnetic resonance imaging is a non-invasive imaging technique that is routinely used for diagnosis and prognosis of patients with congenital heart diseases. Cardiac MRI is also the only modality for high spatial resolution imaging of myocardial viability, myocardial perfusion, and cardiac function and anatomy with excellent soft-tissue contrast in arbitrary imaging planes (24). However, cardiac MRI is challenged with different complexities such as cardiac and respiratory motion compensation and the required expertise needed for accurate image acquisition. This chapter discusses the techniques that are currently used for cardiac imaging in different anatomical imaging planes and the techniques used in cardiac functional imaging including cardiac and respiratory motion compensation techniques.

3.1 Cardiac Imaging Planes

The standard tomographic imaging planes are axial, coronal and sagittal imaging planes. In clinical cardiac MRI, however, images are typically acquired in standard oblique and double oblique imaging planes based on the desired anatomy. The standard cardiac imaging planes include: 1) Vertical long-axis (VLA) plane, 2) Horizontal long axis (HLA) plane, and 3) Short-axis plane. Fig. 3.1 shows example images in the different imaging planes as well as the order of obtaining these imaging planes.

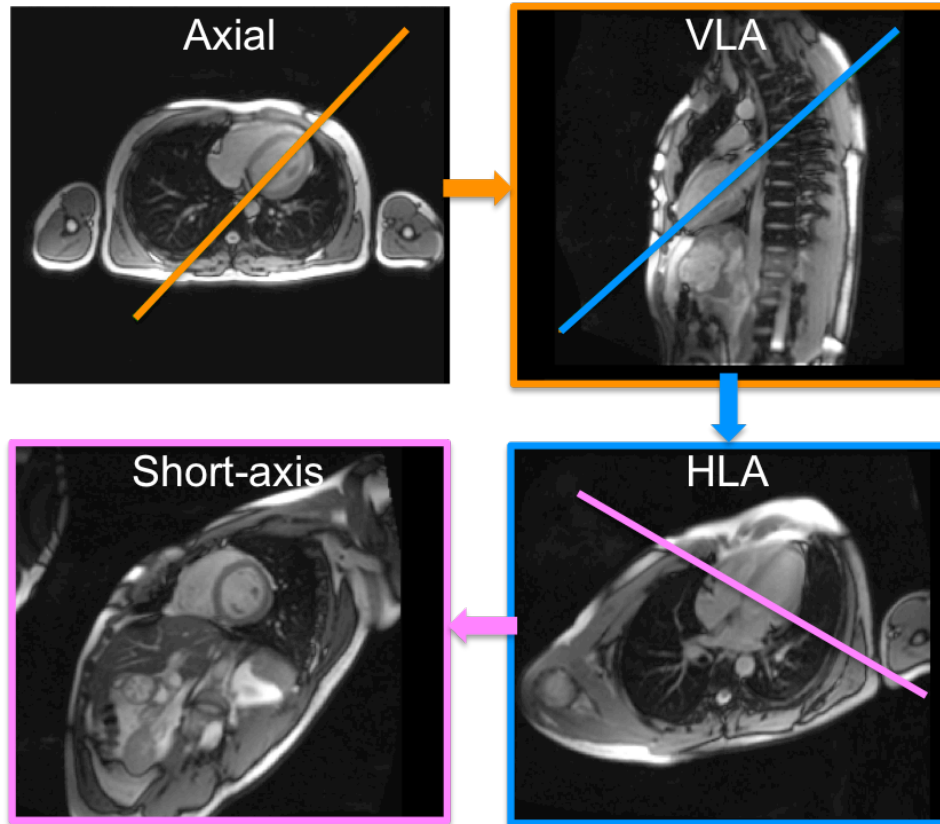


Figure 3.1: Localizer images acquired during cardiac MRI to choose the different imaging planes including the vertical long axis (VLA), horizontal long axis (HLA), and short-axis images. The VLA plane is chosen from the axial localizer image passing through the apex of the heart. The HLA plane is chosen from VLA plane as the plane passing through the apex and the mitral valve. The short-axis plane is chosen to be perpendicular to both ventricles from HLA and VLA views.

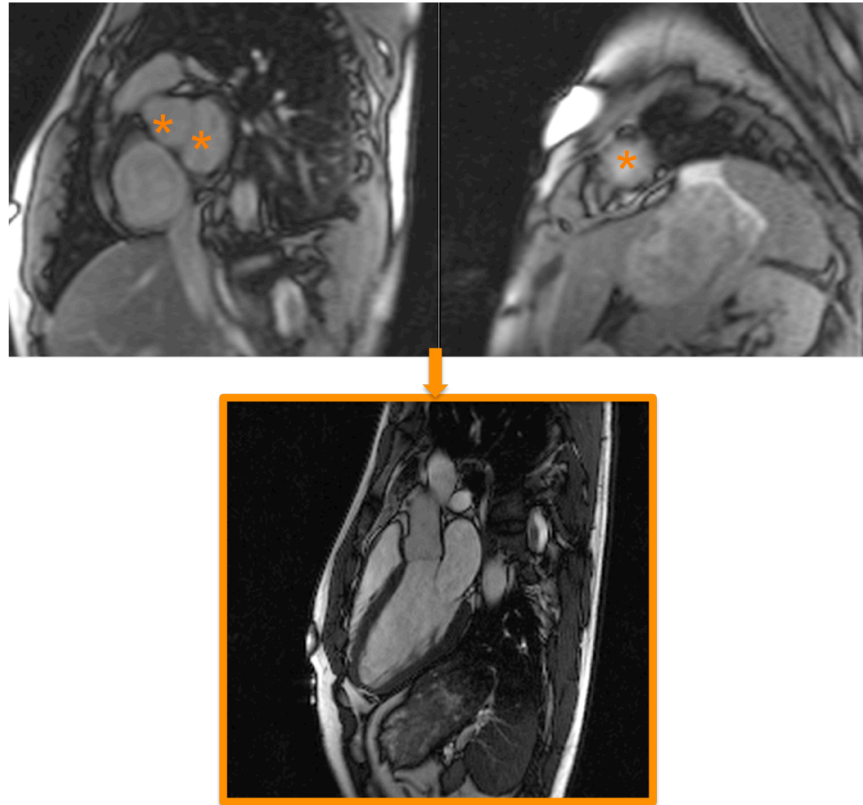


Figure 3.2: The LV out-flow tract (LVOT) plane passes through the mitral valve, aortic valve, and the apex of the heart. These three points (orange stars) are chosen from the multi-slice short-axis images.

Apart, from the above-mentioned imaging planes, there are other anatomy specific imaging planes such as aortic and pulmonary outflow tracts, aorta, branch pulmonary arteries, coronary arteries and specific valve views. Fig. 3.2 shows an example image of Left Ventricular Outflow Tract or the LVOT plane used in Chapter 4.

3.2 Motion Compensation in Cardiac Imaging

The heart moves periodically due to both cardiac motion and respiratory motion. Since, MRI requires several tens of seconds to acquire images, cardiac MRI should compensate for both cardiac and respiratory motion to reduce motion artifacts. The three or four lead electro-

cardiogram (ECG) signal is used to synchronize the MRI signal acquisition to the phase of the ECG, thereby reducing cardiac motion artifacts. However, a clear ECG signal can be difficult to obtain at higher magnetic field strengths ($\geq 3T$) due to the magnetohydrodynamic effect. This effect is due to flowing blood (an ionic solution) through the static magnetic field, which generates an electric signal that corrupts the measurement of the cardiac tissue depolarization. Several other techniques including self-gating (25), acoustic gating (26), are being developed for high field cardiac motion compensation.

Respiratory motion compensation is performed during cardiac MRI using several techniques. For adult patients, if the cardiac MRI acquisition duration is less than about 15-20 seconds the patients are provided instructions to hold their breath during the MRI acquisition either in the end-inspiration or end-expiration respiratory phase. However, in children under around 8 years of age, intravenous sedation or general anesthesia (27) with endotracheal intubation is used to enable external control of breath hold to reduce motion artifacts.

Longer cardiac MRI exams can be performed with free-breathing by tracking the diaphragm or the abdomen position to perform respiratory motion compensation. The two-dimensional diaphragm position can be tracked using cross beam navigators (28) or pencil beam navigators (29). The abdomen position can also be tracked using a pressure sensor (bellows) tied to the abdomen (30). Using either of these techniques, the MR signal is acquired during the same respiratory phase for respiratory motion compensation. Both the 2D navigator echoes and bellows gating monitor the motion of the diaphragm or the abdomen rather than the cardiac motion directly due to the respiration. Respiratory induced cardiac motion compensation can also be performed by directly monitoring the motion of the low resolution three-dimensional images of the heart after each QRS complex (31).

3.3 Cardiac Function Imaging

Cardiac function imaging is routinely performed to measure the global function of the heart and for quantitative measurements of stroke volume, ejection fraction, myocardial mass, cardiac output, end diastolic volume, and end systolic volume. Traditionally, cardiac function imaging was performed using spoiled gradient echo imaging, where in-flow of blood through the imaging plane resulted in higher blood signal and hence good blood-myocardium contrast. However, the blood myocardium contrast was poor in patients with poor cardiac function as well as in imaging planes such as long-axis plane where the in-flow of the blood through the imaging slice was poor. The current clinical standard for cardiac function imaging is using bSSFP due to its T_2/T_1 weighting and hence improved blood-myocardium contrast. The different phases of the heart are acquired by synchronization to the ECG signal as ECG triggered acquisitions or retro-gated acquisitions using segmented k-space acquisition.

3.3.1 ECG Triggered Acquisitions

ECG triggered acquisitions refer to the acquisition of the cardiac phases for a fixed duration from the QRS trigger pulse. The desired number of cardiac phases is acquired using a segmented k-space acquisition as shown in Fig. 3.3. After each ECG trigger, one segment (e.g. 5 to 10 k-space lines) for each cardiac phase is acquired and this process is continued until all segments of k-space are acquired. Note that in the ECG triggered acquisitions the last few cardiac phases (late diastole) of the heart are frequently not acquired because it is difficult to anticipate the precise duration of each cardiac cycle.

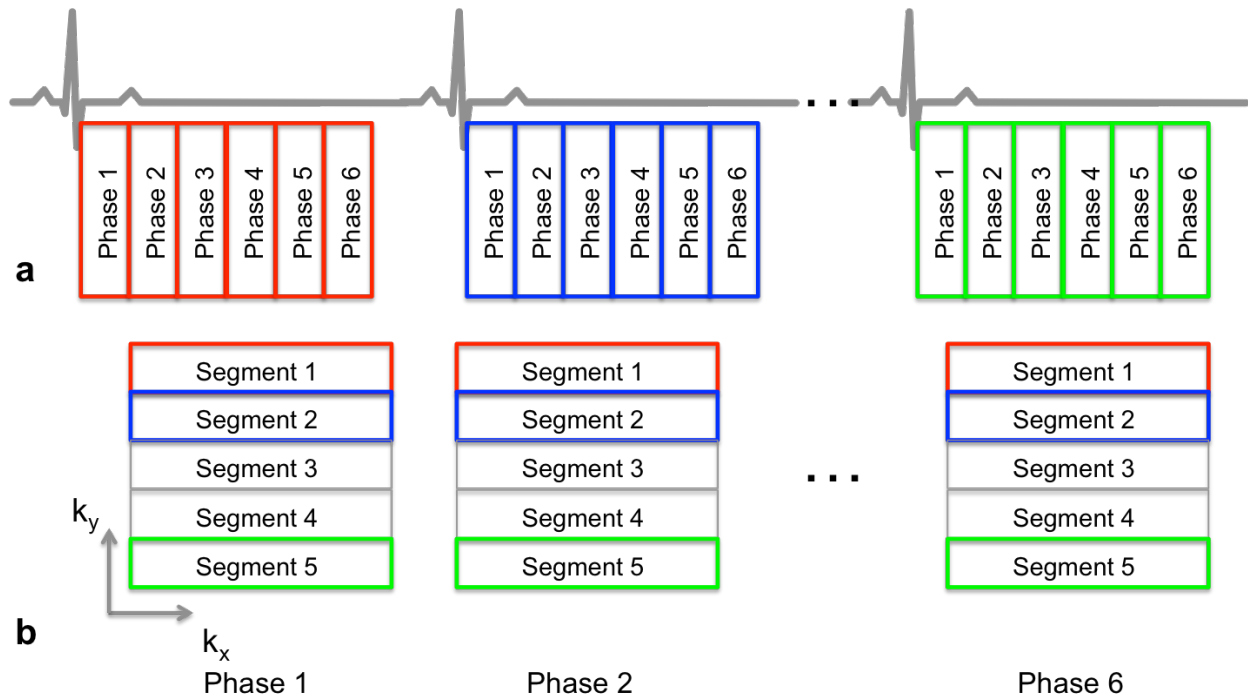


Figure 3.3: Subsequent to the detection of the QRS complex, a single segment of k-space is acquired repeatedly for different cardiac phases (e.g. phase 1, phase 2, etc.) for a fixed duration ($< R-R$ interval) (a). Each cardiac phase is reconstructed from the signal acquired from five consecutive R-R intervals in the shown example (b).

ECG triggered acquisitions are clinically used for imaging that requires preparation pulses such as fat saturation, tagging, inversion recovery. The preparation pulses are applied immediately after the QRS complex, followed by the cardiac cine (or non-cine) acquisition for a fixed duration. The preparation pulse and the imaging pulses are acquired after each QRS trigger, until all the segments of the k-space are acquired.

3.3.2 Retro-gated ECG Acquisitions

Retrospectively gated (i.e. retro-gated) ECG acquisitions are used to acquire images during the entire cardiac cycle including the late diastolic phases. This is also a segmented k-space acquisition where each new segment is acquired in every RR interval. However, the cardiac

phases are acquired continuously until the next QRS trigger unlike ECG triggered acquisitions. Note that due to variations in the RR interval (Fig.3. 4), the number of cardiac phases acquired in each RR interval may vary (Fig. 3.5).

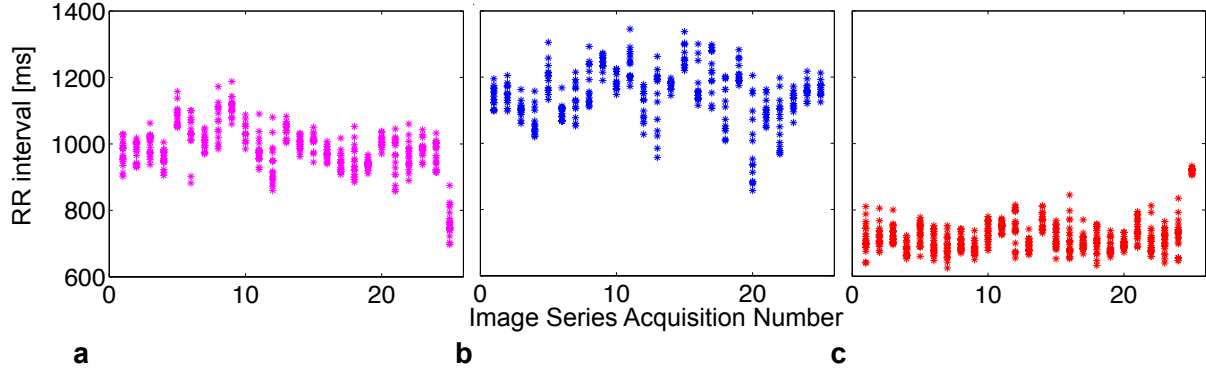


Figure 3.4: RR-interval variations in three different healthy subjects (a, b and c) during 15 seconds breath-hold for 25 consecutive image acquisitions acquired within ~ 1 hour. The different points in the same column indicate the RR variation within a 15 seconds breath-hold. Note that the RR-interval varies significantly both within an acquisition as well as between acquisitions. Hence, linear or bilinear interpolation techniques are necessary for reconstruction of retro-gated cardiac cine acquisitions.

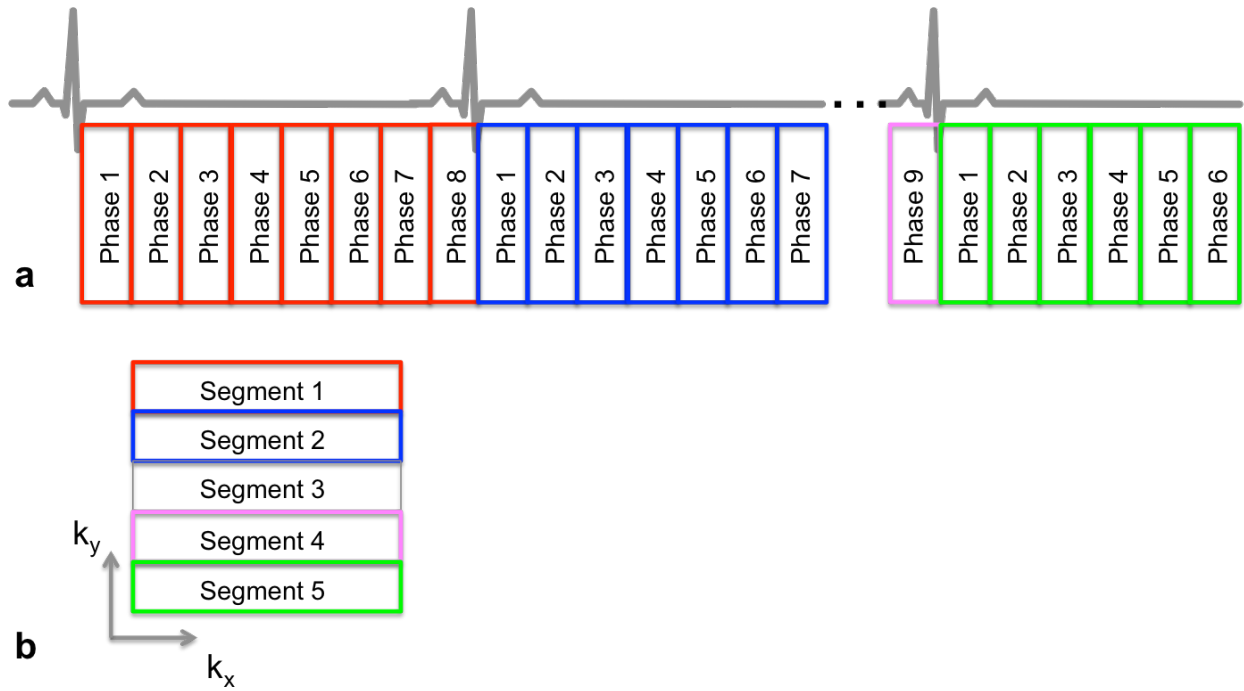


Figure 3.5: In retro-gated ECG cardiac imaging, new k-space segment is acquired in each RR interval and the k-space lines are acquired continuously until the next QRS trigger when the subsequent segment is acquired for all the cardiac phases. The number of segments acquired per RR interval is variable as a consequence of heart rate changes, hence the acquired data needs to be interpolated in order to reconstruct a fixed number of cardiac phases.

Hence the acquired k-space signal has to be interpolated before reconstructing the different cardiac phases. Each k-space line is linearly interpolated to the desired number of cardiac phases and the k-space lines corresponding to each cardiac phase are reconstructed into individual images. Bilinear interpolation techniques (32) can also be used to reduce the image artifacts in diastolic images due to variations in the RR interval.

CHAPTER 4

OPTIMAL FLIP ANGLE FOR CARDIAC CINE IMAGING

Cardiac cine imaging is routinely performed for assessment of global and regional cardiac function. This requires sufficient blood-myocardium contrast to assess the myocardial motion as well as for quantification of ejection fraction, ventricular volumes, ventricular mass and cardiac output. The blood-myocardium contrast depends on several factors including the T_1 and T_2 properties of the tissue, patient-specific percent blood flow (spin replacement) per TR, imaging plane, flip angle, TE/TR and off-resonance. The optimal flip angle for cardiac cine bSSFP, however, remains incompletely characterized.

The optimal flip angle for high blood-myocardium contrast in bSSFP cardiac cine imaging, in the previous literature (33), were based on Bloch equation simulations of stationary myocardium and stationary blood with perfect slice profile and on-resonance magnetization. However, the flow effects in bSSFP (Chapter 2.6), slice profile imperfections alter the optimal FA for high blood signal. In this work, Bloch equation simulations were performed with blood flow effects, imperfect slice profile and off-resonance to determine the optimal FA for high blood-myocardium contrast in cardiac cine imaging. Cardiac cine images were also acquired in healthy subjects and patients with a range of ejection fraction in short-axis, three and four-chamber long-axis planes to determine the flow dependent optimal FA in each of these planes and compared to simulations. *High blood-myocardium contrast can be obtained with a FA $\sim 105^\circ$ when imaging a plane with predominantly through-plane flow such as the short-axis plane. However, if through-plane flow is limited, as may occur for patients with low ejection fraction or low heart rates or four-chamber and three-chamber imaging planes, then the FA should be limited to $\sim 75^\circ$.* This work, titled “Optimal Flip Angle for high contrast balanced SSFP cardiac cine imaging” has been published in Magnetic Resonance in Medicine, 2014; doi:10.1002/mrm.25228. This work was also, in part, presented at ISMRM, Salt Lake City, 2013, abstract: 4574.

4.1 INTRODUCTION

Cine magnetic resonance imaging is routinely performed for the clinical assessment of cardiac structure and function using balanced steady state free precession (bSSFP) imaging. bSSFP cardiac cine imaging is preferred over conventional spoiled gradient echo (SPGR) imaging due to its high signal to noise ratio (SNR), high SNR efficiency, and high blood-myocardium contrast to noise ratio (CNR) (24,34). Conventional SPGR cardiac cine imaging largely depends on the inflow of blood to generate blood-myocardium CNR (35), whereas the blood-myocardium CNR in bSSFP imaging depends on both inflow and out-of-slice effects (23), the tissue T_2/T_1 ratio as well as on repetition time (TR) and flip angle (FA). The strong dependence of the blood-myocardium CNR in bSSFP imaging on the T_2/T_1 ratio is especially useful for imaging patients with poor cardiac function and low blood inflow enhancement (24). The high blood-myocardium CNR in bSSFP also enables automatic myocardial segmentation (36) and improved accuracy of ventricular mass quantification (37). The SNR of bSSFP imaging is also higher than traditional SPGR techniques due to the fully refocused (i.e. balanced) gradients and balanced RF phase cycling (8,38) during each pulse repetition time (TR), which enables magnetization recycling without the need for spoiling.

Maximizing both SNR and CNR are desirable as they lead to improvements in image quality that can improve diagnostic accuracy, produce images that can be automatically segmented with greater robustness, and when in excess make high acceleration rates with parallel imaging or compressed sensing judicious. Bandwidth and TR have minimal influence on the SNR and CNR of bSSFP (39) sequence. Hence, we sought to investigate the flip angle that produces optimal SNR and CNR for cardiac cine imaging with bSSFP with constant bandwidth and TR. Bloch equation simulations can be used to optimize the imaging parameters to produce high SNR or high blood-myocardium CNR. Previous Bloch equation simulations of stationary blood and stationary myocardium with perfect slice profiles at 1.5T and 3T indicate that the optimal flip

angle for high blood-myocardium contrast is 54° and 42° respectively (33), however these values are not in good agreement with clinical experience. This is because the in vivo myocardial signal varies significantly compared to Bloch simulations with a perfect slice profile due to important dependencies on slice profile imperfections and B_0 and B_1 inhomogeneities (40). The in vivo blood signal also varies considerably due to the dependence on the imperfect slice profile, flip angle, flow profile, inflow effects, and out-of-slice (23,41) effects.

Therefore, our *objective* was to define the FAs corresponding to the maximum myocardial signal, maximum blood signal and the maximum blood-myocardium contrast using detailed Bloch equation simulations that included the effects of imperfect slice profile, flip angle, inflow effects, and out-of-slice flow effects and compare these with in vivo measurements of the blood and myocardium SNR and the blood-myocardium CNR in short-axis, four-chamber and three-chamber imaging planes. We *hypothesized* that the optimal FA for maximum blood-myocardium contrast was higher than 54° at 1.5T and was dependent on the imaging plane due to the differences in blood inflow characteristics.

METHODS

4.2 Bloch Equation Simulations

Bloch equation simulations were performed in MATLAB (The Mathworks, Natick, MA, USA). A hamming windowed sinc RF pulse with duration=1200 μ s with a time bandwidth product=1.6 was simulated for a range of FAs between 15° and 180° in steps of 15° . The RF pulse simulation parameters matched the in vivo image acquisition (see 4.3 In Vivo Imaging Experiments). The RF pulse duration was increased to 1200 μ s compared to the conventional 1000 μ s for all the FAs to reduce the specific absorption rate (SAR) of the sequence and allow in vivo imaging at higher FA (approximately $>80^\circ$). The signal characteristics of the imperfect slice profile due to the chosen RF pulse were calculated by simulating 600 sub-slices (N_s) within the imaging slice. A high N_s was chosen to sample the sharp transitions in the slice profile of higher

FAs. The magnitude and the phase of the slice profile (Fig. 4.1a-b) was determined by calculating the magnitude and phase of the transverse magnetization of the RF excitation pulse using a spinor representation of the rotations of the sampled RF pulse (42). As expected, the slice profile deteriorates for $FA > 90^\circ$ due to the chosen pulse duration and time bandwidth product required for short TR, which is needed to reduce the off-resonance artifacts as well as the breath-hold duration. The phase of the slice profile varies linearly within the imaging slice for all the FAs except the 180° . The FA corresponding to each of the 600 sub-slices within the slice was determined by inverse sine of the slice profile (Fig. 4.1c).

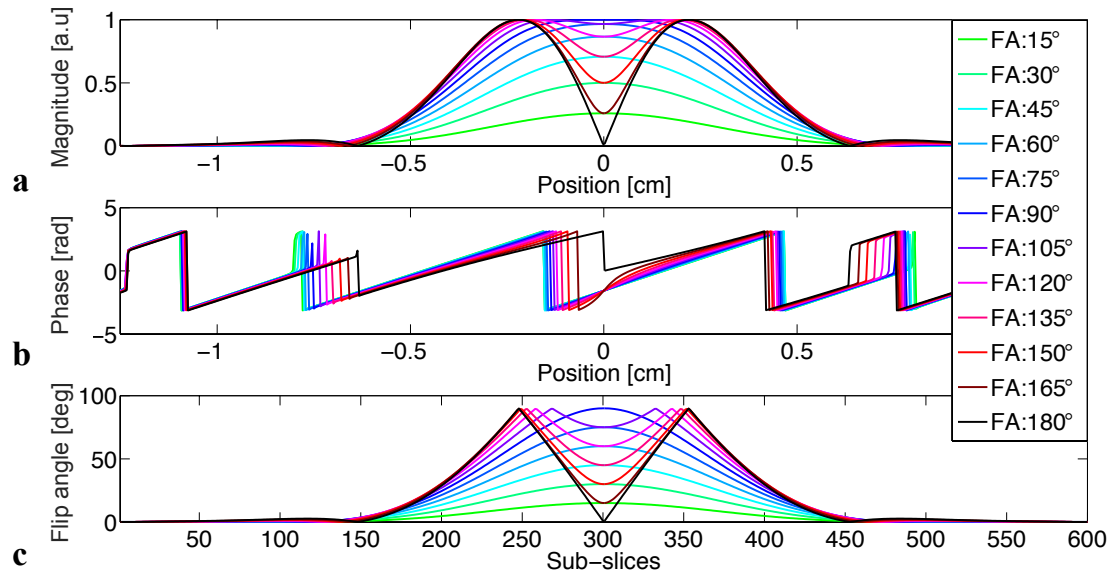


Figure 4.1: The magnitude (a) and phase (b) of the slice profile of the RF pulse for different FAs 15° - 180° in steps of 15° (green to black) with respect to the slice position measured in cm. The slice profile over the imaging slice becomes poor for high flip angles due to short RF pulse duration and short bandwidth time product used for fast bSSFP cardiac cine imaging. The flip angles calculated from the slice profile for different sub-slices ($N_s=600$) is shown in (c).

One dimensional bSSFP signal with respect to the echo number was simulated using a train of equally spaced RF pulses with identical parameters as mentioned above, with constant FA and alternating RF phase for on-resonance spins. The signal was calculated for each of the sub-slices with their corresponding FA, individually for each echo number. The bSSFP signal simulation parameters were TR= 4.4 ms, echo time (TE)= 2.2 ms, $N_{\text{echoes}} = 600$ and for a range of FAs between 15° and 180° in steps of 1° . The simulations were performed for stationary myocardium (T_1/T_2 : 1030/40 ms) (43) and stationary blood and flowing blood ($T_1/T_2/T_2^*$: 1441/290/145 ms) (43) at 1.5 T. A longer TR and TE were used in the simulations to match the in vivo experiments (see below) to reduce the SAR of the sequence without significantly changing the contrast. The spin density of the myocardium and blood was $M_{0\text{myo}}=0.7$ and $M_{0\text{blood}}=0.95$ (33), respectively.

The flow simulation was performed for both blood and myocardium and followed the previous work of Markl *et al.* (23) with a percent spin replacement per TR (Δs) ranging from 0% (no flow) to 100%. For example, $\Delta s=50\%$ and $\Delta s=100\%$ corresponds to a velocity of 56.8 cm/s and 113.2 cm/s respectively for flowing blood or moving myocardium through a slice thickness of 5mm and TR of 4.4ms. The inflow effects were simulated by replacing Δs spins within the imaging slice (N_s) with full magnetization every TR assuming a unidirectional steady plug flow of fresh blood or myocardium. The out-of-slice flow effects were simulated by tracking up to number of out-of-slice, $N_{os}=3 \times \Delta s \times N_s \times T_2^*/TR$, sub-slices outside the imaging slice until their signal decayed by T_2^* effects. The bSSFP signal was calculated individually for all the N_s and N_{os} sub-slices every TR, as the absolute value of the transverse signal. Hence, the calculated signal included effects of both inflow and out-of-slice flow effects. The steady state bSSFP signal was calculated as the average signal of all the N_s and N_{os} sub-slices of the last echo (600th TR).

Simulations of stationary myocardium, stationary blood and flowing blood with $\Delta s=50\%$ were also performed with different off-resonances ranging from 15° to 180° in steps of 15° . Identical

simulations of stationary myocardium ($T_1/T_2=1471/47$ ms), stationary blood and flowing blood ($T_1/T_2/T_2^*=1932/275/138$ ms) with perfect and imperfect slice profiles were simulated for comparison of the optimal FA required for high blood-myocardium contrast at 3T. The signal increases as B_0^2 and hence to compare the myocardium and blood signal with 1.5T, the M_0 of the blood and myocardium at 3T were scaled by four resulting in $M_{0\text{myo}}=2.8$ and $M_{0\text{blood}}=3.8$.

4.3 In Vivo Imaging Experiments

Our Institutional Review Board approved the protocol. All images were acquired on a 1.5T scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) using a six-channel anterior cardiac coil and six-channel posterior spine matrix.

A 2D breath-hold cardiac exam was performed in ten normal subjects ($N=10$, 9 male, age: 28 ± 3 years) subsequent to obtaining informed written consent. 2D segmented, retrospectively ECG gated, mid-ventricular short-axis and four-chamber cardiac cine images were acquired using bSSFP with FAs of 15° - 180° in 15° steps. The highest FA (180°) was not acquired in 6 subjects due to SAR limitations. The imaging parameters were as follows: field of view= 380×296 mm, acquisition matrix= 256×200 , resolution= $1.5\times1.5\times5$ mm, TE/TR= $2.2/4.4$ ms, bandwidth= 501 Hz/px, views-per-segment= 14 - 16 , retrospectively interpolated $N_{\text{phases}}=20$ and $1200\mu\text{s}$ windowed sinc RF pulse with a time bandwidth product of 1.6. The RF pulse duration was increased to $1200\mu\text{s}$ compared to the conventional $1000\mu\text{s}$ for all the acquisitions to reduce the SAR of the sequence and allow imaging at higher FA (approximately $>80^\circ$). The bandwidth was decreased, which increases the TE and TR without significantly changing the contrast and permitted the use of higher FAs within SAR restrictions. Parallel imaging was not used in order to simplify the SNR comparison. The individual acquisition duration depended on the heart rate during the image acquisition and averaged 12 ± 1 s.

Cardiac cine images were also acquired in seven patients ($N=7$, 4 male, age: 32 ± 12 years) in the three chamber LV outflow tract (LVOT) plane with bSSFP and FAs of 45° , 75° and 105° in

addition to a short-axis stack bSSFP cine images which were used to measure ejection fraction. The imaging parameters were identical to those used in the healthy subjects.

4.4 In Vivo Data Analysis

The SNR of the interventricular septum, the right ventricular (RV) blood, and LV blood were measured using ROI analysis. The mean signal intensity within septal, RV, and LV ROIs was calculated for each systolic phase (at ~30% of the cardiac cycle) and each diastolic phase (~90% of the cardiac cycle) for both slice orientations and for each individual. The standard deviation of the background noise was also measured within a region outside the body that was free of any artifacts. The SNR was calculated as the ratio of the mean signal to the standard deviation of the background noise. The SNR was divided by a correction factor (4) of $\sqrt{\frac{2}{4-\pi}} = 1.53$, to account for the Rayleigh distribution of the noise. The CNR was calculated as the SNR difference between the RV or LV blood and the septum. SNR and CNR calculations for RV and LV blood and myocardium were also performed in the LVOT plane for each patient. The LV ejection fraction was calculated subsequent to manual contouring of the multi-slice short-axis acquisition for each patient by an experienced MRI technologist.

Comparison of the Bloch simulation and measured data

The stationary myocardial and flowing blood signal ($\Delta s=50\%$) simulation were collectively scaled to best fit the experimentally measured septal, RV blood, and LV blood SNR for the short-axis and four-chamber views in healthy subjects based on a linear least squares fit between all the simulations and the mean experimental SNR. The stationary myocardial signal simulation was chosen because the average velocity is zero for the periodic myocardial motion. The root mean square error (RMSE) was calculated for the septum, LV blood, and RV blood. The RMSE was calculated as the square root of the ratio of the sum of squares of the

differences between the fitted simulations and the measured values to the number of experiments with different FAs. The coefficient of variation of the RMSE was calculated for the septum, LV blood, and RV blood as the ratio of the RMSE to the mean of simulated and the experimental values.

4.5 RESULTS

Simulations

The Bloch simulation results for myocardium and blood for a range of FAs with different flow velocities and a perfect slice profile are shown in Fig. 4.2a-b. At 1.5T, the maximum stationary myocardium signal was 0.07 and occurred at a FA of 22°; the maximum stationary blood signal was 0.22 and occurred at 48°; and the maximum stationary blood-myocardium signal difference (i.e. contrast) was 0.18 and occurred at a FA of 55° which is in agreement with Schar *et al* (33). In the presence of through-plane flow ($\Delta s > 0$) with a perfect slice profile the maximum flowing blood signal, the maximum moving myocardial signal, and the maximum contrast between stationary myocardium and flowing blood occurred at FA of 90°. At 3T with a perfect slice profile the maximum stationary myocardium signal was 0.28 and occurred at a FA of 20°; the maximum stationary blood signal was 0.8 and occurred at 42°; and the maximum stationary blood-myocardium contrast was 0.15 and occurred at a FA of 47°.

Fig. 4.2d-f highlight the importance of incorporating an imperfect slice profile for simulating the signal response of myocardium and blood. The maximum stationary myocardial signal occurred at 45°, the maximum stationary blood signal occurred at 135° and the maximum contrast of 0.08 between stationary myocardium and stationary blood with imperfect slice profile occurred at 135°. For moving myocardium, with an imperfect slice profile, the maximum myocardial signal occurred in the FA range of 105° to 120°. For flowing blood ($\Delta s > 0\%$) with an imperfect slice profile the contrast between stationary myocardium and flowing blood increases to a range of 0.21 to 0.17 for a FA of 105° to 120° and thereafter decreases slightly. At 3T with

an imperfect slice profile the maximum stationary myocardial signal occurred at 30°, the maximum stationary blood signal at 135° and the maximum flowing blood signal occurred for a FA of 105° to 120°.

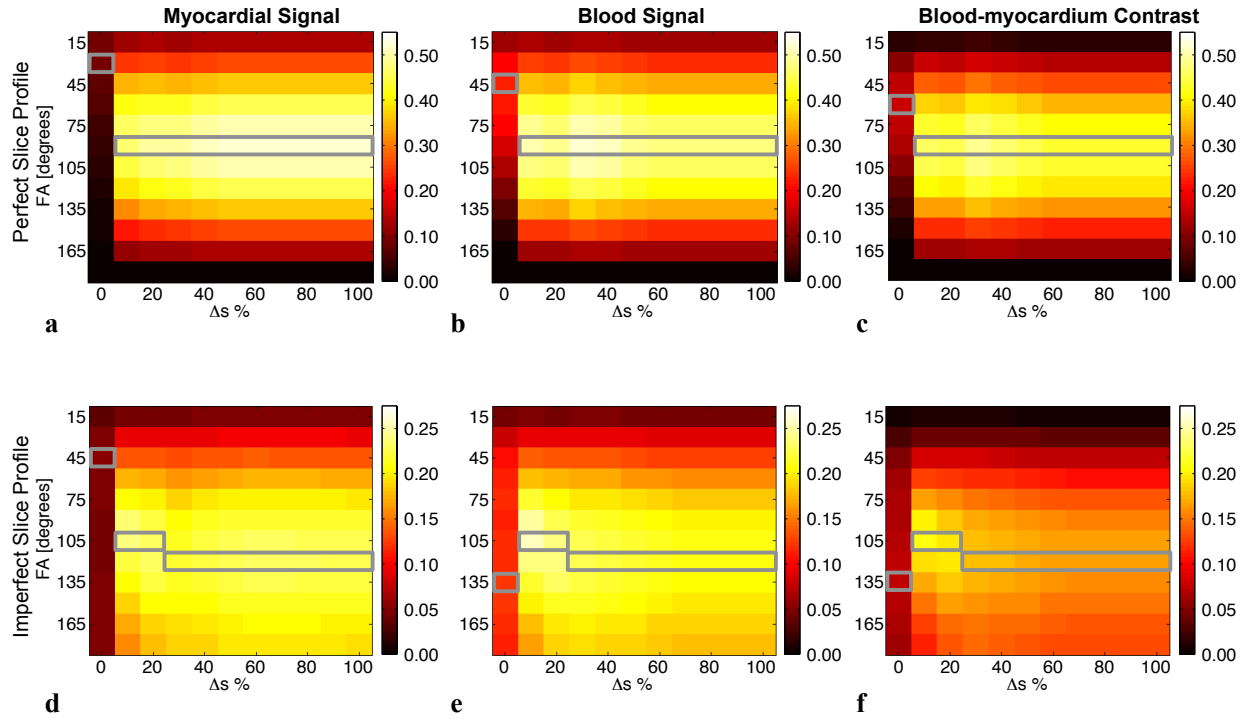


Figure 4.2: Bloch simulations with perfect slice profile of myocardium (a) and blood (b) with different spin replacements per TR (Δs) ranging from 0% (stationary) to 100% (complete replacement of spins within the imaging slice). The contrast between blood with different spin replacements per TR and stationary myocardium is shown in (c). Identical signal simulations of myocardium (d), blood (e) and blood-myocardium contrast (f) were performed with imperfect slice profile. Note that scale of bottom row figures is half the scale of the top row. The solid gray border indicates the maximum signal for each Δs .

The influence of off-resonance on the signals for stationary myocardium, stationary blood, and flowing blood ($\Delta s=50\%$) with an imperfect slice profile is shown in Fig. 4.3a-c. For flowing blood, the signal increases with both increasing off-resonance and increasing FA with an increase in the signal up to $\sim 13.9 \cdot M_0$ with 180° off-resonance, which accords with the values reported by Markl et al (23). The flowing and stationary blood signal, however, is weakly dependent on off-resonances less than 90° .

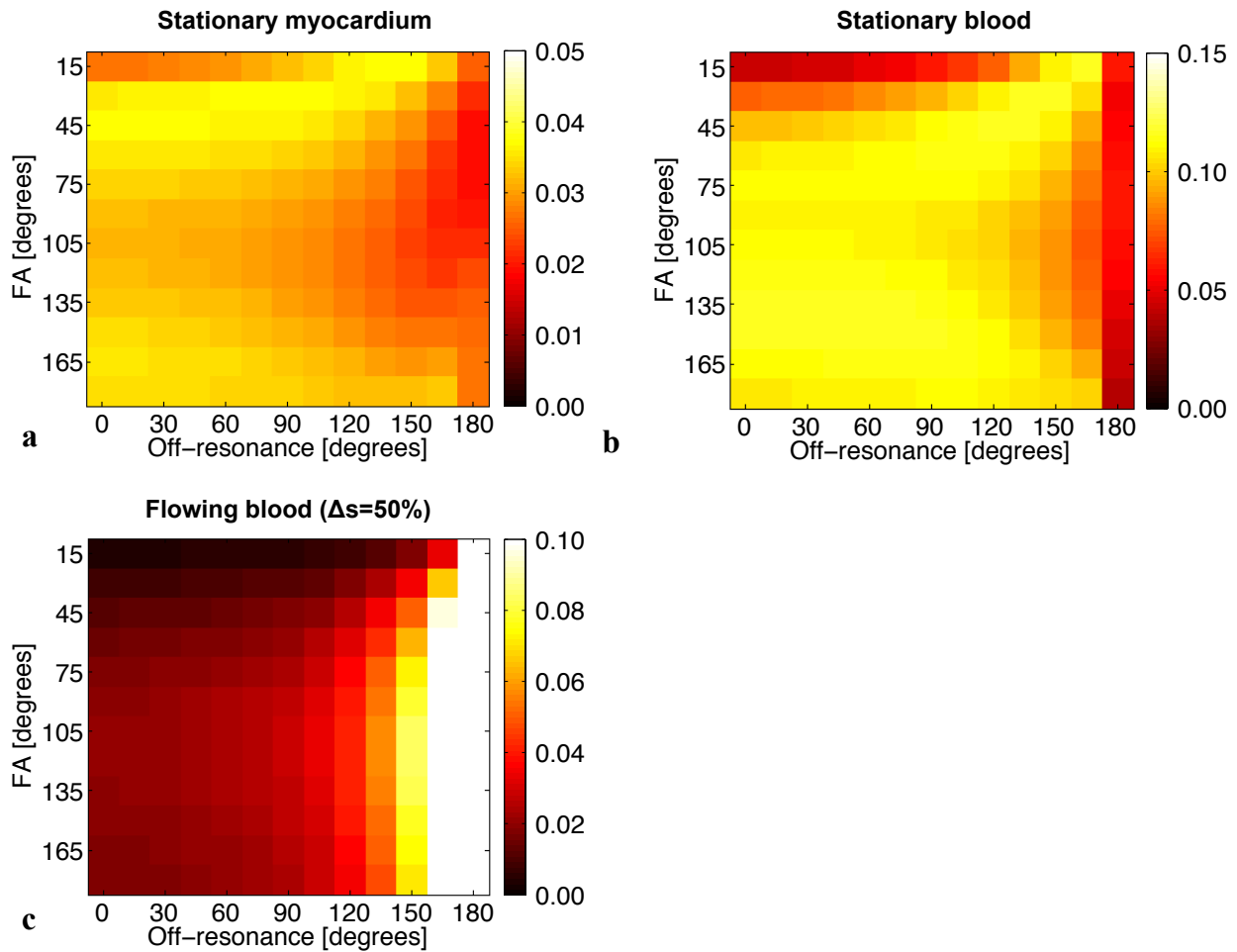


Figure 4.3: Bloch simulations of stationary myocardium (a), stationary blood (b) and flowing blood with $\Delta s=50\%$ (c) and different off-resonance in degrees along x-axis. Note that the scale of the (b) and (c) are three times and ten times respectively of the scale of (a).

In Vivo Analysis in Healthy Subjects

Fig. 4.4a shows a subset of the acquired diastolic and systolic short-axis cardiac images for a healthy subject with flip angles ranging from 15° to 165° in steps of 30° . The mean and standard deviation of the SAR calculated over the 10 subjects is reported in Fig 4.4a. Images from ten subjects were used to report the measured LV blood, RV blood, and myocardial SNR as well as the LV blood-myocardium CNR, and RV blood-myocardium CNR for diastolic and systolic phase, as shown in Fig. 4.4b-e. The myocardial SNR increases up to 30° in diastolic phase and 45° in systolic phase and slightly decreases with increasing FA. The in vivo LV blood and RV blood SNR and the LV and RV blood-myocardium CNR increases with increasing FA. The LV and RV blood SNR and CNR are similar to each other in the systolic phase for all FAs and minimal differences in their SNRs are apparent for $FA > 105^{\circ}$ in the diastolic phase. The RMSE coefficient of variation between the simulated flowing blood and the mean in vivo LV blood SNR is 0.15 during diastole, 0.23 during systole, and 0.21 in the RV blood during diastole and systole. The RMSE coefficient of variation between stationary myocardium and the in vivo septal SNR is 0.27 during diastole and 0.33 during systole.

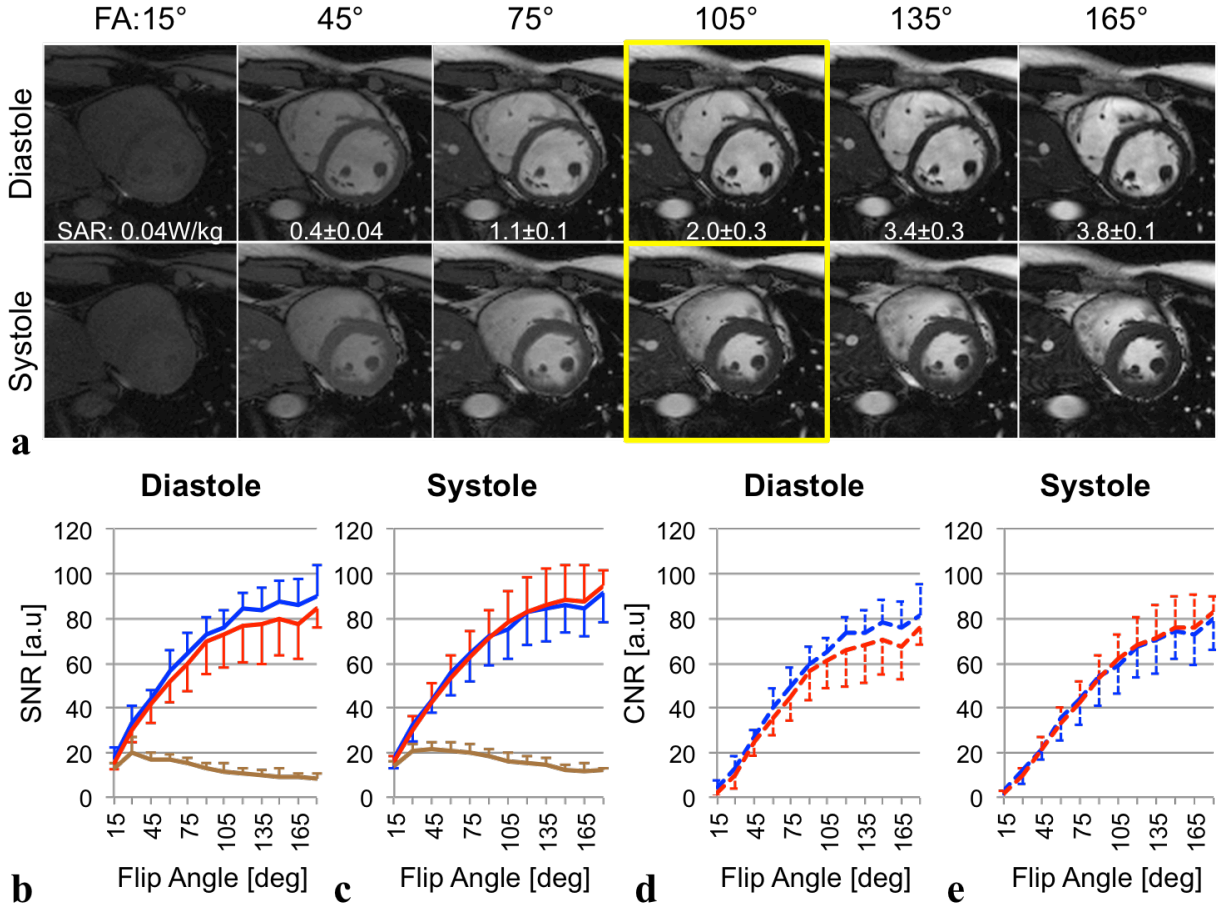


Figure 4.4: a) Diastolic (top row) and systolic (bottom row) images of short-axis bSSFP cardiac cine images of a healthy subject with different FAs from 15°-165° in steps of 30°. The mean SNR of LV blood (red), RV blood (blue) and myocardium (brown) measured during diastole (b) and systole (c) and LV blood myocardial CNR (red dashed) and RV blood myocardial CNR (blue dashed) during diastole (d) and systole (e) show that the blood SNR and blood-myocardium CNR increases with increasing FA, but the increase in blood SNR and CNR for FA > 105° is minimal.

Fig. 4.5a shows a subset of the acquired diastolic and systolic four-chamber cardiac images for a healthy subject with flip angles ranging from 15° to 165° in steps of 30°. The mean and

standard deviation of the SAR calculated over the 10 subjects is reported in Fig 4.5a. The measured LV blood, RV blood, and myocardial SNR, LV and RV blood-myocardium CNR in the diastolic and systolic phases is shown in Fig. 4.5b-e respectively. The myocardial SNR increases up to 30° in diastolic phase and 45° in systolic phase and slightly decreases with increasing FA similar to the short-axis images. The RV blood SNR and RV blood-myocardium CNR during systolic and diastolic phases is similar to the short-axis plane. However, the LV blood SNR and LV blood-myocardium CNR increases for increasing FA up to $\sim 75^\circ$ and remains relatively constant for $FA > 75^\circ$. Consequently, the difference in SNR and CNR between the LV blood and RV blood increases with increasing FA and is more evident in the systolic phase (Fig. 4.5c,e) than the diastolic phase (Fig. 4.5b,d). The coefficient of variation of the RMSE between the simulated flowing blood and the mean measured LV blood signal is 0.31 during diastole and 0.47 during systole. The coefficient of variation of the RMSE for the RV blood signal is 0.11 during diastole and 0.17 during systole. The RMSE coefficient of variation between stationary myocardium and the in vivo septal SNR is 0.22 during diastole and 0.24 during systole.

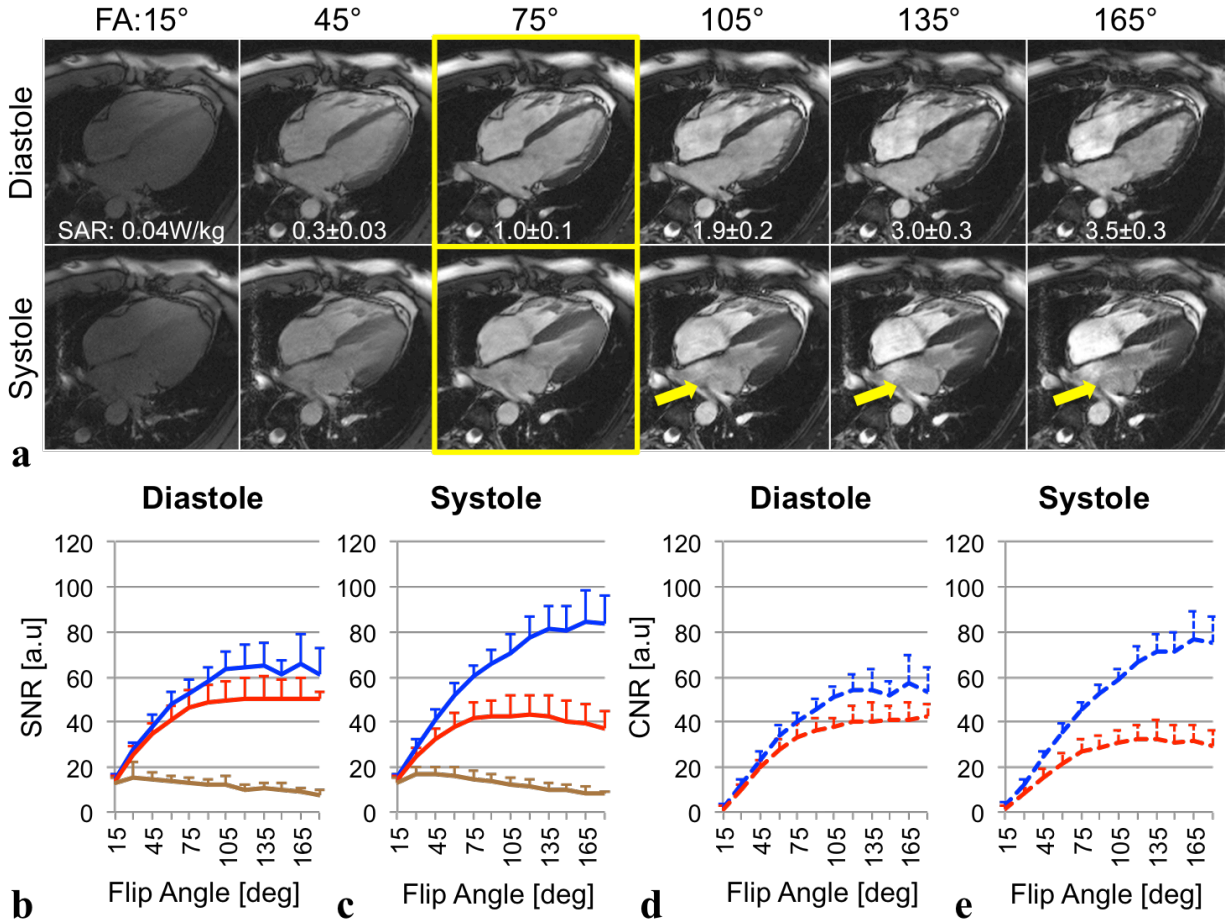


Figure 4.5: a) Diastolic (top row) and systolic (bottom row) images of four-chamber bSSFP cardiac cine images from a healthy subject with different FAs from 15°-165° in steps of 30°. The mean SNR of LV blood (red), RV blood (blue) and myocardium (brown) measured during diastole (b) and systole (c), LV blood myocardial CNR (red dashed) and RV blood myocardial CNR (blue dashed) during diastole (d) and systole (e) indicate that at higher FAs, the blood signal is decreased in the LV compared to the RV due to the blood signal saturation of the pulmonary veins with long acquisition durations. Blood SNR and blood-myocardium CNR differences are clearly visible in the systolic phase (arrows) at higher FAs (a) and measured LV and RV mean blood SNR and blood-myocardium CNR (c,e).

In Vivo Analysis in Patients

The ejection fraction (EF) and heart rate of the patient during cardiac cine acquisition determine, in part, the flow of blood within and through the imaging plane. Fig. 4.6a compares systolic images in the LVOT plane for two patients with similar heart rates (74 vs. 77 beats/min), but different EF (37.1% vs. 58.4%) acquired with FA=45°, 75° and 105°. The LV blood-myocardium CNR and RV blood-myocardium CNR measured during systole and diastole are shown in Fig. 4.6b-c. The CNR for FAs of 75° and 105° is higher than the CNR with FA of 45° in all the patients. Of note, however, there is minimal difference between the LV blood-myocardium CNR for FAs of 75° and 105° in patients with low EF or low heart rate.

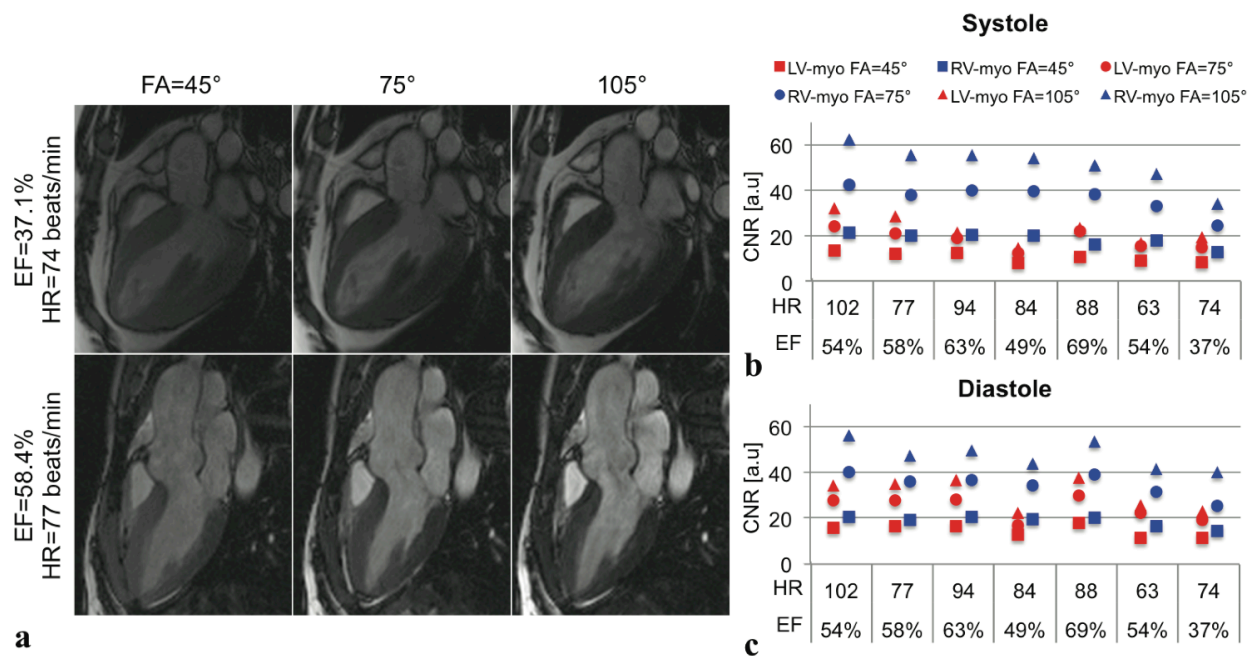


Figure 4.6: a) Three chamber view (LVOT) images of two different patients with (top) low ejection fraction (EF)=37.1% and (bottom) normal EF=58.4% and similar heart rates (HR) of 74 vs. 77 beats/min acquired at FA=45°, 75° and 105°. The LV blood-myocardium CNR (red) and RV blood-myocardium CNR (blue) were measured in seven patients at FA=45° (square), 75° (circle) and 105° (triangle) during systole (b) and

diastole (c). RV blood-myocardium CNR exceeds LV blood-myocardium CNR due to the differences in through-plane versus in-plane flow. CNR values also tend to be lower for subjects with low EF and/or low HR.

4.6 DISCUSSION

In the short-axis view the measured in vivo LV and RV blood SNR in both the systolic and diastolic phases increases with increasing imaging FA. The percent increase in SNR is >10% for every 15° increase in FA over the range of 15° to 105° and decreases with further increase in FA. Bloch simulations of flowing blood and stationary myocardium signal that use an imperfect slice profile and account for out-of-slice flow effects corroborate this finding and indicate that the blood signal increases with increasing FA up to ~105°-120° and decreases slightly thereafter, whereas the stationary myocardial signal is relatively constant over a wide range of FAs (>=45°). Hence, to achieve the highest blood-myocardium contrast cardiac cine imaging in the short-axis plane within SAR constraints the highest possible FA up to 105°-120° should be used.

For the four-chamber view, the measured RV blood SNR in both systolic and diastolic phases is similar to the simulated flowing blood signal and similar to the LV and RV blood SNR in the short-axis plane. Note, however, that at higher FAs (>75°), the four-chamber LV blood SNR and CNR is lower than the RV blood SNR and CNR. This likely arises as a consequence of the saturation of the blood signal in the pulmonary tissue and veins within the imaging plane that drains into the left chambers of the heart. This saturation leads to reduced in-flow effects and diminished blood signal intensity in the left chambers of the heart. Similarly, in the LVOT view the RV blood flows predominantly through-plane compared to the LV blood flow, which largely circulates in-plane. As a consequence, the RV blood signal is noticeably higher than the LV blood signal for FA=105° in patients with normal EF or high heart rate.

In summary, high SNR short-axis cardiac cine images can be acquired with FAs as high as 105° - 120° , beyond which the SNR gains are limited and SAR becomes problematic. The SNR gain between $FA=75^{\circ}$ and $FA=105^{\circ}$ depends, in part, on the EF and heart rate of the patient and may be limited in patients with low EF and/or low HR (Fig. 4.6b-c). Images in the four-chamber view and three-chamber view have high and uniform blood SNR in both the RV and LV up to 75° beyond which there is increased signal differences between the RV and LV blood, which may be undesirable. Bloch simulations and measured diastolic LV blood in the four-chamber plane indicates that a FA of 75° will increase the blood-myocardium CNR (by $\sim 21\%$) compared to the previously reported optimal FA of 54° . Similarly, for 3D cardiac cine applications where the blood signal is reduced due to signal saturation (44), a higher FA up to 75° need to be used to improve the blood-myocardium contrast. Simulations of stationary blood with imperfect slice profile (Fig. 4.2e) suggest that increasing FA beyond 75° up to 135° will only incrementally increase the blood-myocardium contrast, but incur substantially higher SAR.

Cardiac cine imaging, however, may be SAR-limited as the FA approaches 105° , especially with a short TR. Variable FA cardiac cine imaging (45) can be used to lower the SAR of the sequence, while maintaining the use of an effectively higher FA in order to obtain increased blood-myocardium contrast in the short-axis plane. Parallel imaging techniques like GRAPPA (46) and SENSE (47) can also be used to reduce the acquisition duration and hence reduce the overall SAR of the imaging sequence, which then permits the use of a higher FA.

The flowing blood signal was simulated for a range of velocity up to 116 cm/s and was relatively independent of the through plane velocity, which accounts for the apparent blood-signal homogeneity in vivo for which a wide range of velocities are present. The optimal FA was higher for simulations using imperfect slice profiles (FA of 105° to 120°) compared to perfect slice profiles ($FA=90^{\circ}$) due to the reduction in the average FA within the imperfect slice profile despite the same nominal FA. In the flow simulations with an imperfect slice profile it is apparent that the prescribed FA had to be increased beyond 90° in order to achieve the maximum signal

by way of increasing the average FA. For the chosen RF pulse (see 4.2 Methods), the highest average FA within the imaging slice was 79.3° , which occurred at the prescribed FA of 105° .

The RMSE coefficient of variations in the short-axis imaging plane between the simulation and the in vivo LV and RV blood was in the range of (0.15-0.23). The higher values were due to the inconsistency between the simulation and the in vivo values at high FA ($>135^\circ$) where the simulation indicated a slight reduction in the signal and the in vivo results suggested an increase in the signal. In the four-chamber imaging plane, the RMSE coefficient of variations between the simulated flowing blood and the mean in vivo SNR for the LV blood (0.31-0.47) was higher than that of the RV blood (0.11-0.17), which was likely due to the inflow saturation of the LV blood from the pulmonary veins – an effect that was not simulated. However, the RMSE coefficient of variations between stationary blood simulation and mean LV blood was 0.08 during systole and 0.14 during diastole suggesting that the lower in vivo SNR was partly due to blood signal saturation as a consequence of in-plane flow. The RMSE coefficient of variations for the myocardium was high (0.22-0.33) in both four-chamber and short-axis imaging planes. This was partly due to the stationary myocardial signal simulation with imperfect slice profile (Fig. 4.3a) which has a nearly constant signal for $FA > 45^\circ$ whereas the in vivo myocardial SNR decreases with increasing FA for $FA > 90^\circ$. However, the stationary myocardium simulations with off-resonance indicated that the signal decreases at higher FAs for increased off-resonance, which were not considered in the RMSE calculation due to lack of the B_0 map.

The simulations were based on sinc RF pulses with a pulse duration and time bandwidth product matched to the parameters of the product sequence. As a consequence, the slice profile for each different FA was sub-optimal. The RF pulses for different FAs can be individually optimized for their slice profile and SAR using SLR (42) and VERSE (48,49) pulse design which will reduce the optimal FA results to more closely align with the simulations that used a perfect slice profile.

Limitations

The TR of the imaging sequence was specifically increased to 4.4ms to reduce the SAR and enable imaging at high FAs. In practice, the TR of the imaging sequence is minimized to reduce sensitivity to B_0 inhomogeneities and the related banding artifacts for bSSFP cardiac cine imaging. Our simulations and preliminary experiments in 5 healthy subjects with FA up to 80° and TR=3.1ms (data not reported) demonstrated a similar trend in the myocardial and blood signal compared to those acquired with TR=4.4ms. The myocardial and blood signals at TR=3.1ms, however, were slightly higher than at TR=4.4ms, but did not shift the optimal FA. Nevertheless, whenever possible the use of a high FA is preferred to increase blood-myocardium contrast, while staying within SAR limits.

The flow simulations considered only in-flow effects due to through plane flow. Further improvements to these simulations are required to incorporate the periodic motion of the myocardium and define the optimal FA for the myocardium. The differences in the blood signal between the LV and the RV blood as well as between the different cardiac phases and different imaging planes are due to the flow effects such as in-plane flow and blood signal saturation due to re-circulating spins. Further improvements to the flowing blood simulations would be required to account for these patient specific flow effects.

4.7 CONCLUSION

Bloch equation simulations of flowing blood and stationary myocardium with an imperfect slice profile agree well with the measured blood-myocardium CNR in the short-axis and four-chamber imaging planes in healthy subjects. High blood-myocardium CNR can be obtained with a FA $\sim 105^\circ$ when imaging a plane with predominantly through-plane flow such as the short-axis plane and increasing the FA beyond 105° results in limited SNR and CNR gains compared to the quadratic increases in SAR. When imaging planes with both through-plane flow and in-plane flow such as the four-chamber and three-chamber imaging planes, if uniform blood SNR is

desired in both the LV and RV, then the maximum FA should be limited to $\sim 75^\circ$. Finally, if through-plane flow is limited, as may occur for patients with low ejection fraction or low heart rates, then the FA may similarly be limited to $\sim 75^\circ$.

CHAPTER 5

VARIABLE FLIP ANGLE IMAGING

Variable flip angle (VFA) imaging techniques are being used to either reduce the SAR during image acquisition (50-52) or to maintain a constant signal during image acquisition to improve the spatial resolution (53) as well as to modify the image signal (54) and contrast (55,56). In this chapter, several variable flip angle techniques used in both spin echo imaging as well as bSSFP imaging are reviewed.

5.1 Transition between Pseudo Steady States (TRAPS)

Spin echo (SE) and turbo spin echo (TSE) techniques use 180° refocusing pulses for complete refocusing of the signal. However, application of 180° pulses are SAR intensive especially at high field strengths ($\geq 3T$). Hence, variable flip angle techniques can be used to reduce the SAR of TSE imaging. However, the use of variable flip angle results in signal oscillations, lower signal and image artifacts. These limitations were overcome using preparation pulses to systematically increase the signal to a pseudo steady-state signal (57,58).

The variable flip angle scheme for TRAPS (50) spin echo imaging, uses these pre-calculated preparation pulses to reach static pseudo steady state for a given refocusing flip angle. The imaging FA scheme varies from a lower flip angle ramping up to 180° , when the center of k-space is acquired, followed by ramping down of the flip angle to a lower FA to reach a pseudo steady-state. The use of lower refocusing flip angles in spin echo imaging, allows an increase in the number of refocusing pulses after each excitation pulse and reduces the SAR as well. As the center of the k-space is acquired with a 180° refocusing pulse, the signal is mostly T_2 weighted due to the spin echoes. The use of refocusing pulses lower than 180° , results in the generation of both spin echoes and stimulated echoes which may change the overall signal and contrast of the image.

5.2 Variable Flip Angle Spin Echo Imaging with Constant Transverse Magnetization

Variable flip angle schemes for the refocusing pulses have also been designed to maintain constant transverse magnetization during image acquisition that improves the image sharpness by reducing the k-space signal weighting (52,59). Using extended phase graphs (EPG) and a prospective EPG algorithm, the VFA train is designed to maintain a constant signal for a particular tissue and improve the image sharpness compared to constant flip angle spin echo acquisitions.

5.3 Improved SNR bSSFP Imaging at 3T

bSSFP images are acquired with a short TR at high field strengths to reduce the off-resonance artifacts. The need for a short TR in addition to increased optimal FA of bSSFP, increases the SAR, which can become limiting at 3T. A variable flip angle scheme (54) can be used to reduce the SAR of bSSFP imaging. The VFA approach can also permit the use of higher flip angles to improve the SNR of the images at 3T with constant SAR. The VFA scheme can, for example, enable the use of a maximum FA of 40° to 48° compared to maximum allowed constant flip angle of 34° with constant SAR and constant TR. Similar to the TRAPS acquisition, the maximum FA is used to acquire the center of k-space for increased SNR with a penalty on image blurriness due to the k-space weighting introduced by the VFA scheme. This VFA scheme is further explored in low SAR or high contrast cardiac cine imaging in Chapter 6.

5.4 T_2 -TIDE bSSFP Imaging

VFA techniques are also used to modify the image contrast. Eqn. 2.6 in Chapter 2 indicates that with FA of 180° , the transient signal in bSSFP can be purely T_2 weighted. In T_2 -TIDE imaging (55), the center of k-space is acquired using 180° pulses for T_2 weighting, and one side of the high spatial frequency k-space lines is acquired by smoothly ramping down the FA to a lower

value of about 60° . As the bSSFP signal reaches a steady state value at this lower flip angle, the higher k-space lines will have steady signal, which is unlike the complete decay of the signal observed in spin echo imaging. The T_2 weighting is controlled by varying the number of 180° pulses before the center k-space is acquired. Fig. 5.1a shows the VFA scheme with the order of k-space acquisition used for T_2 -TIDE imaging. Fig. 5.1b shows simulation of the T_2 -TIDE signal compared to pure T_2 decay of a tissue with $T_1/T_2=1000/90$ ms, bSSFP high FA= 180° , bSSFP low FA= 60° , TR=4.5ms, TE=TR/2 and number of echoes=120. Due to the steady state signal of bSSFP at FA= 60° , the high spatial frequency k-space lines can be acquired with a high signal to improve the image sharpness. The negative high spatial frequency k-space is filled using partial fourier reconstruction. Hence, T_2 -TIDE images are comparatively sharper than the fast spin echo images like HASTE. This T_2 weighted bSSFP VFA scheme is further explored in Chapter 8 for T_2 weighted prostate imaging at 3T. Due to the off-resonance effects of fat in bSSFP imaging, a similar T_2 -TIDE VFA schemes can also be used for fat signal saturation (60).

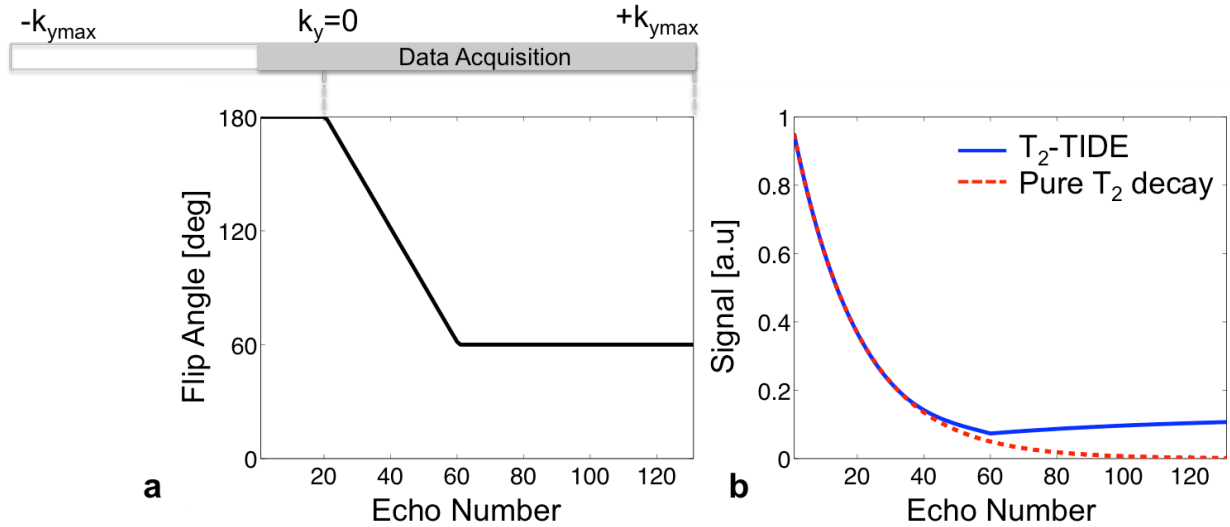


Figure 5.1: a) The flip angle (FA) scheme of the T_2 -TIDE sequence starts with a 90° preparation pulse followed by a set of 180° preparation pulses and then the acquisition of a few negative low spatial frequency k-space lines with FA= 180° up to the center of k-space. The FA is then ramped down to a lower FA during the acquisition of the high

positive spatial frequency k-space lines. (b) Simulation of the T_2 -TIDE signal (blue) as a function of echo number for a tissue with $T_1/T_2=1000/90$ ms, $TR=4.5$ ms with the VFA scheme in (a) compared to pure T_2 decay (red). The T_2 -TIDE signal does not decay to zero during the acquisition of the high k-space lines, thereby retaining the edge information while preserving the T_2 weighted signal at the center of k-space.

5.4a Choice of the ramping trajectory for bSSFP Imaging

Several ramping trajectories have been used for smooth signal transition between higher and lower flip angles. The simplest of these ramping trajectories is the linear scheme where the flip angle linearly increases between the two flip angles. However, when N_{ramp} is low ($\sim < 10$) with increased difference between α_{low} and α_{high} , strong signal oscillations remain, resulting in image artifacts (61). These artifacts can be minimized using a modified linear ramping scheme where the first and the last ramp flip angles are stepped by $\Delta\alpha/2$, where $\Delta\alpha$ is the step increment between the flip angles (17).

Non-linear ramping trajectories like Gaussian, sinusoidal, Kaiser-Bessel can also be used for smooth transition between two different flip angles (61). These different trajectories result in transition similar to the modified linear ramping scheme for higher N_{ramp} (> 20).

5.5 Variable-angle Uniform Signal Excitation (VUSE) for bSSFP Imaging

The bSSFP signal requires a long train of pulses of about $5 \times T_1/TR$ for the signal to reach steady-state. If the images are acquired before the steady-state is reached, then the spatial resolution of the image will be reduced due to the k-space weighting. The k-space weighting can be reduced, by predicting the FA required for reaching a particular uniform M_{xy} signal using Bloch equation simulations (53). This improves the spatial resolution of the images and reduces

the preparation duration of bSSFP acquisitions. For a desired transverse magnetization (M_T), the required FA is calculated using (53):

$$\tan \alpha = \frac{2 G_2 G_3 \pm \sqrt{(2 G_2 G_3)^2 - 4(H^2 - G_3^2)(H^2 - G_2^2)}}{2(H^2 - G_3^2)} \quad [5.1]$$

where $G_2 = -E_2 M_{xy}$; $H = \frac{-M_T}{E_2}$; $G_3 = E_1 \cdot M_z + (1 - E_1)M_0$; $E_{1,2} = e^{-\frac{TE}{T_{1,2}}}$

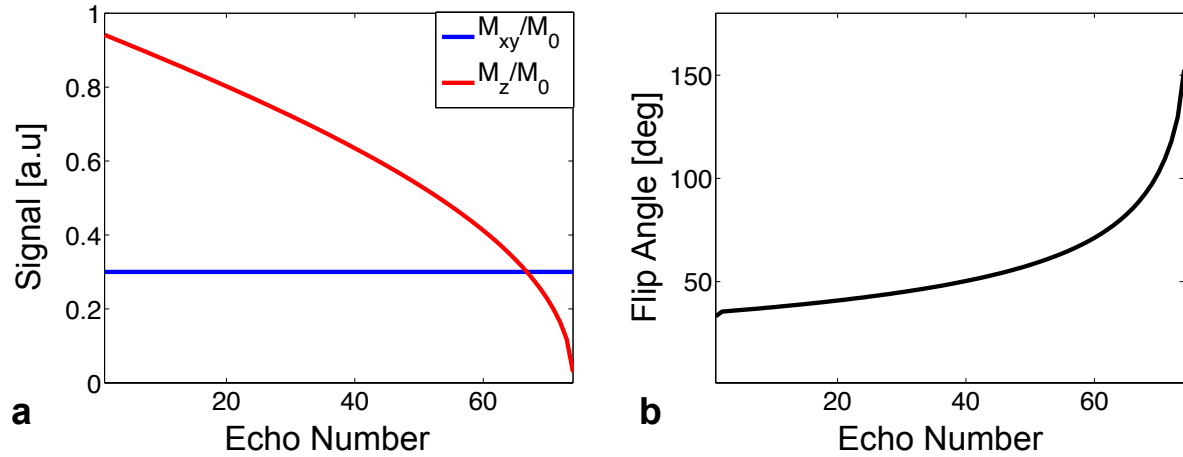


Figure 5.2: a) Simulation of the transverse (blue - M_{xy}/M_0) and longitudinal (red - M_z/M_0) magnetization over the echo number for a tissue with $T_1/T_2=907/50$ ms. The calculated flip angle profile using Eqn. 5.1 to generate the desired constant transverse magnetization (M_T) of 0.3 is shown in (b). The FA increases towards 180° (b) as the longitudinal magnetization approaches zero.

This VFA scheme allows conversion of all the longitudinal magnetization into the transverse magnetization. Hence, neither the transverse or the longitudinal magnetization reach steady-state and will require complete recovery of the signal before subsequent signal acquisition. Fig. 5.2 shows the simulated FA profile for a tissue with $T_1/T_2=907/50$ ms, $TR=3.8$ ms, $TE=TR/2$, $M_T=0.3$ and six Kaiser Bessel preparation pulses to reduce off-resonance artifacts. Note that the FA increases exponentially up to 180° and as the signal is acquired during the

transient state, the images are no longer purely T_2/T_1 weighted. This derivation of VFA scheme is further explored in Chapter 9 for low SAR non-contrast enhanced peripheral arteriography.

CHAPTER 6

LOW SAR OR HIGH CONTRAST VFA bSSFP CARDIAC CINE IMAGING

Cardiac cine images are typically acquired as multiple single-slice breath-held acquisitions that cover the entire left ventricle in the short-axis imaging plane and several long-axis (e.g. two- and four-chamber imaging planes). As a consequence of the work reported in Chapter 4, it was established that the optimal FA for high blood-myocardium contrast cardiac cine bSSFP imaging is in the range of 75° - 120° . Combined with the requirement of using a short TR to reduce off-resonance banding artifacts, results in bSSFP cardiac cine imaging being SAR intensive. These factors can result in sustained heating for a longer time and can be more problematic in imaging conscious pediatric patients who have heightened sensitivity to heating.

Increased SAR is also a problem when imaging patients with implanted devices and poses the highest risk for RF induced lead-tip heating, potential tissue damage and may inhibit pacing and/or ICD shocks (62). Hence, low SAR cardiac cine imaging is a potentially useful approach to improving patient acceptance and a promising technique to reduce the SAR while maintaining the high blood-myocardium contrast.

In this work, we have used a variable flip angle bSSFP scheme similar to Paul et al., (54) as described in Chapter 5.3, to lower the SAR of 2D breath-held, cardiac cine sequence while maintaining similar blood-myocardium contrast. A non-segmented k-space acquisition, asynchronous to the ECG is used to adapt the VFA scheme (VFA-bSSFP), for lower SAR or higher contrast cardiac cine imaging. *The novel aVFA-bSSFP technique can be used to lower the SAR by at least 36% with similar blood-myocardium CNR compared to the conventional bSSFP cardiac cine imaging. aVFA-bSSFP can also be used to increase the CNR by at least 28%, with similar SAR compared to conventional bSSFP.* This work, titled “Variable flip angle balanced steady-state free precession for lower SAR or higher contrast cardiac cine imaging” has been published in Magnetic Resonance in Medicine, 2014; 71(3): 1035-1043. This work was also, in part, presented at ISMRM, Salt Lake City, 2013, abstract: 3713.

6.1 INTRODUCTION

Cardiac cine imaging is routinely performed clinically using balanced steady-state free precession (bSSFP) (24) (i.e TrueFISP, b-FFE and FIESTA) due to its high blood-myocardium contrast-to-noise ratio (CNR) and high signal-to-noise ratio (SNR) efficiency. The blood-myocardium CNR for spoiled gradient echo imaging technique strongly depends on inflow, which can result in low blood-myocardium CNR, especially in patients with impaired cardiac function. The SNR in bSSFP is dependent on the T_2/T_1 values of the tissues. Due to the inherent differences in T_2/T_1 values between myocardium and blood, bSSFP imaging provides higher CNR, even for patients with impaired myocardial function. The bSSFP blood SNR also increases with increasing flip angle (FA) (23) due to the dependence of the blood signal on inflow velocity and out of slice effects (23). The use of higher FAs with a short TR, however, results in substantially increased SAR (W/kg), which limits achievable SNR and CNR and can restrict the use of bSSFP for applications such as imaging patients with implanted devices (e.g. pacemakers and ICDs) and imaging at higher field strengths ($\geq 3T$).

Variable Flip Angle (VFA) imaging approaches have been developed to lower SAR for spin echo imaging (50,63), to obtain T_2 -weighted contrast with bSSFP (55) or SSFP-echo (56) sequences, to increase spatial resolution for bSSFP imaging (53); and to increase SNR in bSSFP (54) and spoiled gradient echo (64) non-cine imaging. All of these techniques have used single-shot or multi-shot imaging, but without application to cardiac cine imaging, which is conventionally acquired using segmented cine k-space acquisitions.

Conventional k-space segmented cardiac cine bSSFP images (Fig. 6.1a) acquire the first k-space segment for each cardiac phase during the first cardiac cycle (R-R interval) followed by the acquisition of the second segment for each cardiac phase during the second cardiac cycle and so on until all k-space segments are acquired. However, various VFA schemes coupled to

segmented k-space acquisitions and bSSFP are not able to reduce the overall SAR of the sequence efficiently and produce significant image artifacts (see Methods).

We propose to use an asynchronous k-space acquisition (Fig. 6.1b) for VFA-bSSFP cardiac cine imaging, which is asynchronous to the cardiac cycle, termed as aVFA-bSSFP. This is equivalent to acquiring multiple single-shot images of the same slice and retrospectively rebinning the k-space data based on the recorded phase of the cardiac cycle. Kellman *et al.* previously used a similar asynchronous k-space acquisition for high resolution free-breathing constant flip angle cardiac cine imaging (65) in order to uniformly sample k-space during different cardiac phases.

Therefore, our **objective** was to develop the aVFA-bSSFP technique specifically for cardiac cine imaging. We **hypothesize** that the aVFA-bSSFP technique can: 1) lower the SAR of cardiac cine bSSFP imaging while maintaining blood-myocardium CNR similar to conventional segmented constant FA bSSFP (sCFA-bSSFP); or 2) increase the blood SNR and blood-myocardium CNR compared to asynchronous constant FA bSSFP (aCFA-bSSFP) with similar SAR.

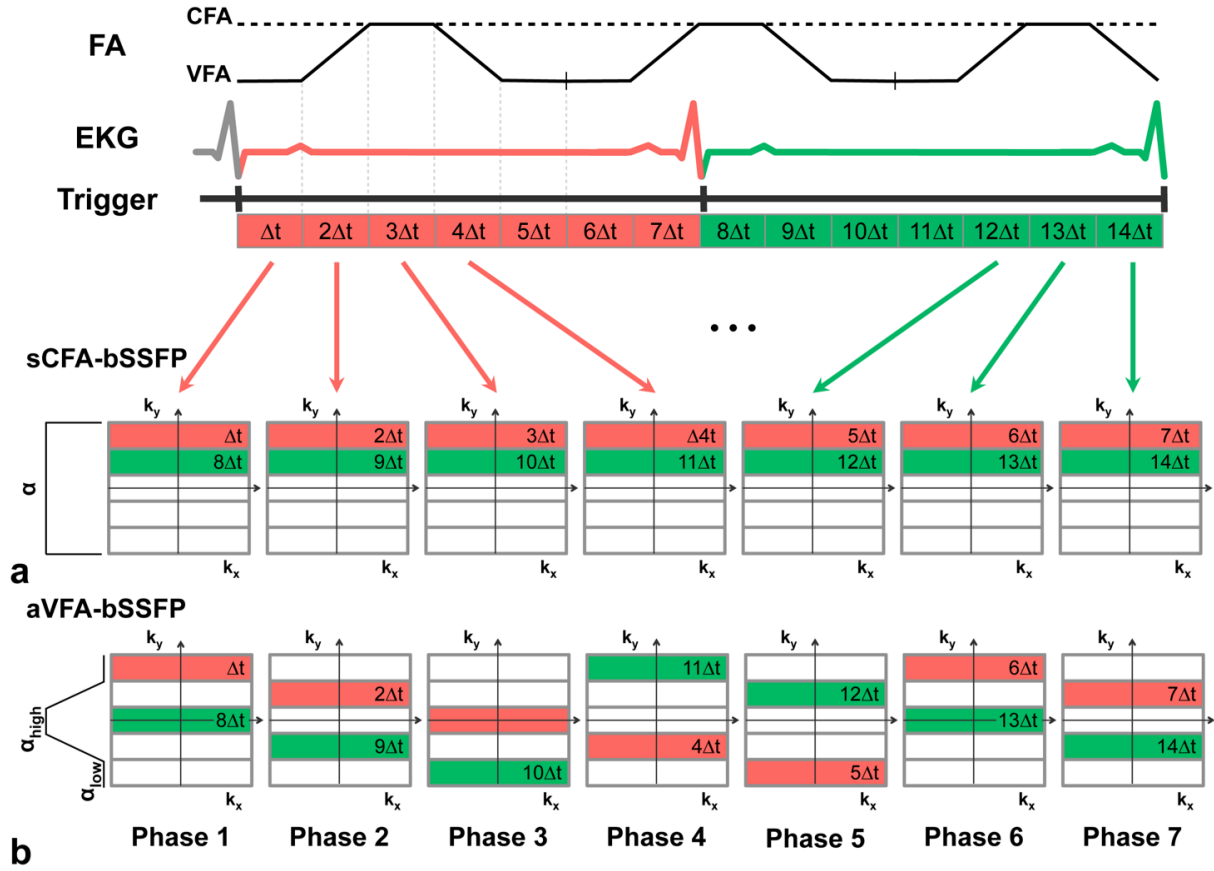


Figure 6.1: Comparison of conventional segmented k-space acquisition (A) to the asynchronous VFA-bSSFP cardiac cine technique (B) showing the k-space acquisition of seven cardiac phases during the first two RR-intervals (red and green). The VFA-bSSFP scheme is asynchronous to the RR-interval as shown on the top. Δt , $2\Delta t$, etc indicate the acquisition order of the different segments where Δt is the acquisition duration for each segment. The VFA-bSSFP scheme varies from α_{low} to α_{high} and back to α_{low} linearly across k-space, which reduces the SAR, while maintaining image contrast.

METHODS

6.2 Design of Flip Angle scheme for VFA-bSSFP

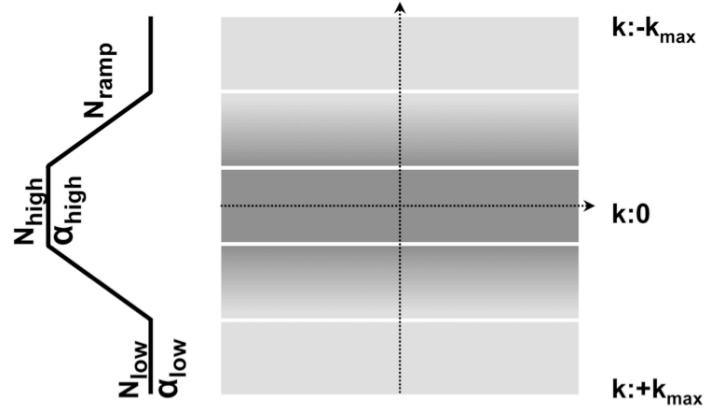


Figure 6.2: VFA-bSSFP uses a trapezoidal FA scheme consisting of five different parameters: lower FA (α_{low}), higher FA (α_{high}), number of low pulses (N_{low}), number of high pulses (N_{high}) and number of linear ramp pulses (N_{ramp}). The α_{low} pulses are used to acquire the outer k-space lines to reduce the SAR, followed by the ramp pulses to catalyze a smooth transition to a higher steady state that uses α_{high} for increased SNR.

The proposed VFA scheme uses a trapezoidal FA history (50) which is defined by five different parameters: a low FA (α_{low}), a high FA (α_{high}), the number of α_{low} pulses (N_{low}), the number of linear ramp pulses (N_{ramp}), and the number of α_{high} pulses (N_{high}) as shown in Fig. 6.2. The combination of these parameters is defined as the number of VFA (N_{VFA}) = $2 \times N_{low} + 2 \times N_{ramp} + N_{high}$. The proposed VFA scheme is designed such that $N_{VFA} = N_{ky}$ where N_{ky} is the number of phase encode steps per shot. Images are acquired using a top-down trajectory such that α_{high} is used to acquire the center of k-space, thereby maintaining the overall SNR and CNR of the image to be similar to conventional bSSFP. The α_{low} pulses accord with the outer k-space lines and therefore reduce the overall SAR of the image acquisition, but concomitantly incur a loss in resolution too. The linear N_{ramp} pulses promote a smooth transition between the

lower (α_{low}) and higher (α_{high}) steady states, which minimizes artifacts. Throughout this paper, a specific VFA scheme is represented as $\alpha_{\text{low}}\alpha_{\text{high}}N_{\text{ramp}}N_{\text{high}}$. For example, VFA scheme 30_70_40_80 is used to represent the scheme with $\alpha_{\text{low}}=30^\circ$, $\alpha_{\text{high}}=70^\circ$, $N_{\text{ramp}}=40$, $N_{\text{high}}=80$. For a fixed, N_{ky} (e.g. $N_{\text{ky}}=204$) we then have $N_{\text{low}} = [N_{\text{ky}} - (N_{\text{high}}+2\times N_{\text{ramp}})]/2=22$. For comparison purposes we also evaluated aCFA-bSSFP sequence that uses the same asynchronous acquisition and reconstruction technique as aVFA-bSSFP.

	$\alpha_{\text{high}}=50^\circ$	$\alpha_{\text{high}}=70^\circ$	$\alpha_{\text{high}}=90^\circ$
$\alpha_{\text{low}}=10^\circ$	10_50_20_40 10_50_40_40 10_50_20_80 10_50_40_80	10_70_20_40 10_70_40_40 10_70_20_80 10_70_40_80 10_70_60_80 10_70_20_100 10_70_40_100	10_90_20_40 10_90_40_40
$\alpha_{\text{low}}=30^\circ$	30_50_20_40 30_50_40_40 30_50_20_80 30_50_40_80	30_70_20_40 30_70_40_40 30_70_20_80 30_70_40_80	
$\alpha_{\text{low}}=50^\circ$	CFA-bSSFP 50	50_70_20_40 50_70_40_40	
$\alpha_{\text{low}}=70^\circ$		CFA-bSSFP 70	

Table 6.1: Twenty-five different VFA-bSSFP and CFA-bSSFP schemes used for simulations and imaging experiments. The VFA-bSSFP schemes in non-bold were used to determine the scheme with blood-myocardium CNR similar to CFA-bSSFP of 50° and bold VFA-bSSFP schemes were used to determine the scheme with blood-myocardium CNR similar to CFA-bSSFP of 70° . The VFA-bSSFP scheme is represented as $\alpha_{\text{low}}\alpha_{\text{high}}N_{\text{ramp}}N_{\text{high}}$.

Twenty-five different aVFA-bSSFP and aCFA-bSSFP schemes (Table 6.1) were evaluated with simulations and imaging experiments to determine which aVFA-bSSFP scheme produced blood-myocardium CNR similar to aCFA-bSSFP of 50° and 70° while reducing SAR and with minimal loss in resolution. The schemes were chosen systematically by varying the VFA-bSSFP scheme parameters: α_{low} was varied from 10° to α_{high} in steps of 20°, N_{ramp} was chosen as 20 or 40, N_{high} was either 40, 80, or 100, α_{high} was 50°, 70°, or 90°. Only VFA-bSSFP schemes with ΣFA^2 (proportional to the SAR of the sequence for a fixed TR) lower than the corresponding CFA-bSSFP sequence were chosen.

6.3 VFA Acquisition Strategy

Various VFA-bSSFP acquisition strategies could be used with a segmented k-space acquisition in order to reduce SAR, but the concomitant artifacts, poor blood-myocardium contrast, and minimal SAR reduction makes each approach unfavorable. For example, the acquisition strategy could vary the FA throughout the RR interval such that $N_{\text{VFA}} = N_{\text{segments}}$ (number of k-space lines acquired within each segment) $\times N_{\text{phases}}$ (number of cardiac phases). However, the center of k-space for the middle cardiac phase would be acquired with a higher FA and consequently would have higher CNR and SNR and the center of k-space for the first and last cardiac phases would be acquired with a lower FA and would have a lower SNR and CNR. This difference in SNR and CNR between cardiac phases is undesirable. Alternately, the FA could vary across each k-space segment such that $N_{\text{VFA}} = N_{\text{segments}}$, but N_{VFA} would be small and consequently would not significantly reduce the SAR and the concomitant signal modulations in the k-space would cause artifacts. Lastly, if the FA was varied over the entire imaging acquisition such that $N_{\text{VFA}} = N_{\text{segments}} \times N_{\text{phases}} \times \text{number of cardiac cycles}$, the images would have ghosting artifacts due to k-space discontinuities that arise as a consequence of rebinning the data acquired during the ramp interval.

To overcome the above problems, we propose using an asynchronous k-space acquisition with $N_{VFA}=N_{ky}$ for VFA-bSSFP where k-space is filled asynchronously with respect to the RR-interval. In each RR-interval, consecutive continuous segments that span all cardiac phases are acquired without synchronization to the cardiac cycle. The asynchronous k-space acquisition is also equivalent to acquiring multiple single-shot images, which are retrospectively re-binned into different cardiac phases. The asynchronous acquisition is unlike the conventional segmented acquisition where the same k-space segment is acquired for all the cardiac phases in each RR-interval. Fig. 6.1 compares the segmented and asynchronous k-space acquisitions during the first two RR-intervals. An asynchronous k-space acquisition with $N_{VFA}=N_{ky}$, avoids the above mentioned limitations (i.e. ghosting, CNR fluctuations, and ineffective SAR reductions) because a continuous k-space acquisition of the different cardiac phases with the consecutive trapezoidal VFA schemes not susceptible to ghosting artifacts, maintains similar SNR and CNR during all the cardiac phases and significantly reduces the SAR.

6.4 Bloch Equation Simulations

Bloch equation simulations were performed in MATLAB (The Mathworks, Natick, MA, USA). Simulations of the transverse magnetization (M_{xy}) as a function of the echo number were performed for stationary myocardium (T_1/T_2 : 867/57 ms), flowing blood ($T_1/T_2/T_2^*$: 1200/200/200 ms) and an aqueous nickel-sulfate phantom (T_1/T_2 : 100/100 ms). Both a conventional CFA-bSSFP sequence of 70° and a 30_70_40_80 VFA-bSSFP scheme were simulated. An imperfect slice profile was simulated with 20 sub-slices (N_s) and a 600 μ s RF pulse with a time bandwidth product of 1.6 similar to Markl *et al.* (23). The slice profile was defined by the Fourier Transform of the RF pulse. The slice profile was divided into 20 sub-slices and the flip angle for each sub-slice was defined by scaling the sub-slice's signal by the central sub-slice's signal. The other simulation parameters were spin density of the myocardium (M_{0myo})= 0.7, (M_{0blood})= 0.95 (33), pulse repetition time (TR)= 3.070 ms, echo time (TE)= 1.535 ms, number of shots (N_{shots})= 5,

and $N_{ky} = 204$. The flow simulation follows the previous work of Markl *et al.* (23) with a percent spin replacement per TR (Δs) of 50% and a number of out-of-slice sub-slices, $N_{os} = 4 \times \Delta s \times N_s \times T_2 / TR$.

Simulations of the myocardial signal and flowing blood signal were also performed for the 25 different VFA-bSSFP and CFA-bSSFP schemes (Table 6.1) with the same simulation parameters explained above. The simulated myocardial and flowing blood signal was calculated as the dynamic steady-state signal of the center echo number from the third shot. The resolution loss incurred by the VFA-bSSFP scheme was estimated for each of the 25 different FA schemes. The point spread function (PSF) was calculated as the Fourier transform of the dynamic steady-state signal of the third shot. The full width half max (FWHM) of the PSF was measured as the width of the PSF at half the maximum value to estimate the resolution loss.

The frequency response of the 30_70_40_80 VFA-bSSFP scheme and a 70° CFA-bSSFP scheme was simulated by calculating the signal for the phantom (T_1/T_2 : 100/100 ms) with off-resonance between -180° and 180° in 5° steps.

6.5 Imaging Experiments

All the images were acquired on a 1.5T scanner (Avanto; Siemens Medical Solutions, Erlangen, Germany) using a 6-channel anterior cardiac coil and 6-channel posterior spine matrix.

Phantom Imaging

A nickel-sulfate phantom (1.25 g of $\text{NiSO}_4 \times 6 \text{ H}_2\text{O}$ + 5 g NaCl per 1000 g of distilled water) was imaged using multi-echo spin-echo experiments to measure T_2 with TR=8000ms and TE=11, 50, 100, 150 and 200ms. The T_1 values were measured using multiple inversion recovery spin-echo experiments. The imaging parameters were: TR = 4000ms, TE = 9.5ms, TI = 10, 50, 75, 100, 120, 200, 300, 400, 500, 1000, 1500 and 3000ms. The values were estimated to be T_1/T_2 :100/100ms by fitting the signal curves. The phantom was imaged with parameters

matched to the simulations (Field of view= 380×302 mm, acquisition matrix= 256×204, resolution= 1.5×1.5×5 mm, TE/TR=1.535/3.070 ms, Bandwidth=1502 Hz/px, $N_{shots}=25$), and VFA-bSSFP scheme (30_70_40_80). Projections were acquired with the phase encoding gradients switched-off in order to evaluate the dynamics of the transverse magnetization with high temporal resolution. The sum of the coil combined signal (using sum of squares technique) along the readout direction was compared to the simulated results.

Resolution phantom experiments were performed on a phantom with different sized disks to qualitatively compare the image sharpness acquired with VFA-bSSFP (30_70_40_80) and CFA-bSSFP (70°). Images of the plastic grid in the ACR MRI accreditation phantom (J M specialty parts, San Diego, CA, USA) were also acquired using the 25 different bSSFP schemes (Table 6.1). To quantify image blurriness the first two shots were discarded and the subsequent images from 23 consecutive shots were averaged to reduce the noise. The blurriness of a single edge of the grid was measured at three different locations similar to Larson et al. (66) by first measuring I_{max} and I_{min} (maximum and minimum image intensity) points on a line profile drawn over the grid along the phase encoding direction, then computing the distance between $0.8(I_{max}-I_{min})+I_{min}$ and $0.2(I_{max}-I_{min})+I_{min}$. The imaging parameters were identical to the stationary phantom experiment.

The frequency response of the CFA-bSSFP (70°) and VFA-bSSFP (30_70_40_80) schemes were experimentally measured by applying a linear shim gradient of 200 μ T/m along the readout direction using the nickel-sulfate phantom with imaging parameters identical to the above experiments. The line profile over the phantom was compared to the simulated frequency response.

In Vivo Imaging

A 2D breath-hold cardiac cine exam was performed in ten normal ($N=10$, 8 male, age: 28 ± 4 years) subjects subsequent to obtaining informed written consent. Our Institutional Review

Board approved the protocol. 2D mid-ventricular short-axis cardiac cine exams were performed using sCFA-bSSFP with FAs of 50° and 70° ($N_{\text{segments}}=16$, $N_{\text{phases}}=25$). The other imaging parameters were identical to the phantom experiments mentioned above. Twenty-five different experiments (Table 6.1) for the same mid-ventricular short-axis slice were acquired with each bSSFP schemes in each volunteer.

The ECG signal was recorded during image acquisition for offline reconstruction of the aVFA-bSSFP and aCFA-bSSFP images. The acquisition duration for both the aVFA-bSSFP and aCFA-bSSFP experiments was 15 s. The acquisition duration for the sCFA-bSSFP acquisitions depended on the heart rate variation during the image acquisition and averaged 12 ± 2 s.

2D short-axis cardiac cine images were also acquired using aCFA-bSSFP with the maximum FA based on the individual patient's SAR limit. A aVFA-bSSFP scheme ($50_\alpha_{\text{high}}_{40_{40}}$, where α_{high} was $98 \pm 1^\circ$) with SAR approximately matched to patient-specific SAR for aCFA-bSSFP ($\alpha=74 \pm 5^\circ$) was also acquired in order to evaluate the potential increase in blood-myocardium CNR using aVFA-bSSFP compared to aCFA-bSSFP with similar SAR.

6.6 Image Reconstruction

The aVFA-bSSFP and aCFA-bSSFP images were reconstructed offline retrospectively, using MATLAB. The first shot consisted of significant signal transients during the approach to steady-state and was discarded during image reconstruction. Subsequently, each k-space line was associated with a normalized time (between 0 and 1) based on its time-of-acquisition with respect to the corresponding RR-interval (cardiac cycle) obtained from the recorded ECG data. Each k_y -line, was then linearly interpolated into 25 cardiac phases, coil combined (sum of squares), 2D Fourier transformed, and the magnitude resulted in 25 cardiac cine images.

6.7 In Vivo Data Analysis

The SNR of the blood and myocardium were measured using ROI analysis. ROIs were drawn over the septum and left ventricular blood of the single shot diastolic images and the mean signal was measured. The interpolated images were not used for this analysis to avoid any complex impact on the measured signal and noise. The standard deviation of the background noise was also measured. SNR was calculated as the ratio of the mean signal to the standard deviation of the noise. Blood-myocardium CNR was calculated as the ratio of signal difference of blood and myocardium to the standard deviation of the noise. A paired student t-test was performed to test for significant differences between the mean blood-myocardium CNR and SAR values obtained for the aVFA-bSSFP and aCFA-bSSFP experiments.

6.8 Comparison of the Bloch simulation and measured data

The experimentally measured values were scaled to best fit the simulation results based on linear least squares fit between all the simulations and mean experimental data. This was performed for the following experiments: 1) simulation versus measured signal phantom 2) simulation versus measured frequency response; and 3) comparison of the simulated blood and myocardial signal and measured blood and myocardial SNR. The correlation coefficient (R) was calculated between the simulated and the mean of the measured experimental data.

6.9 RESULTS

Simulations and Phantom Experiments

The FA schemes for the simulation and phantom experiments of VFA-bSSFP and CFA-bSSFP are shown in Fig. 6.3a. The simulation of the transverse magnetization for the phantom using the VFA-bSSFP and CFA-bSSFP (Fig. 6.3b), demonstrates the repeated dynamic steady-state signal using the VFA-bSSFP scheme and the constant signal of the CFA-bSSFP scheme after

the first ~150 echoes. The measured signal obtained from the nickel-sulfate phantom agrees well ($R = 0.99$) with the simulation confirming the accurate simulation of the dynamic steady-state signal (Fig. 6.3b). Simulation of the myocardium and flowing blood signals for the VFA scheme (Fig. 6.3c) demonstrate a consistent dynamic steady state signal after the first single shot measurement (Fig. 6.3a). The duration of the transverse magnetization signal transient (time to reach steady-state) is slightly shorter using the 30_70_40_80 VFA-bSSFP scheme compared to CFA-bSSFP scheme.

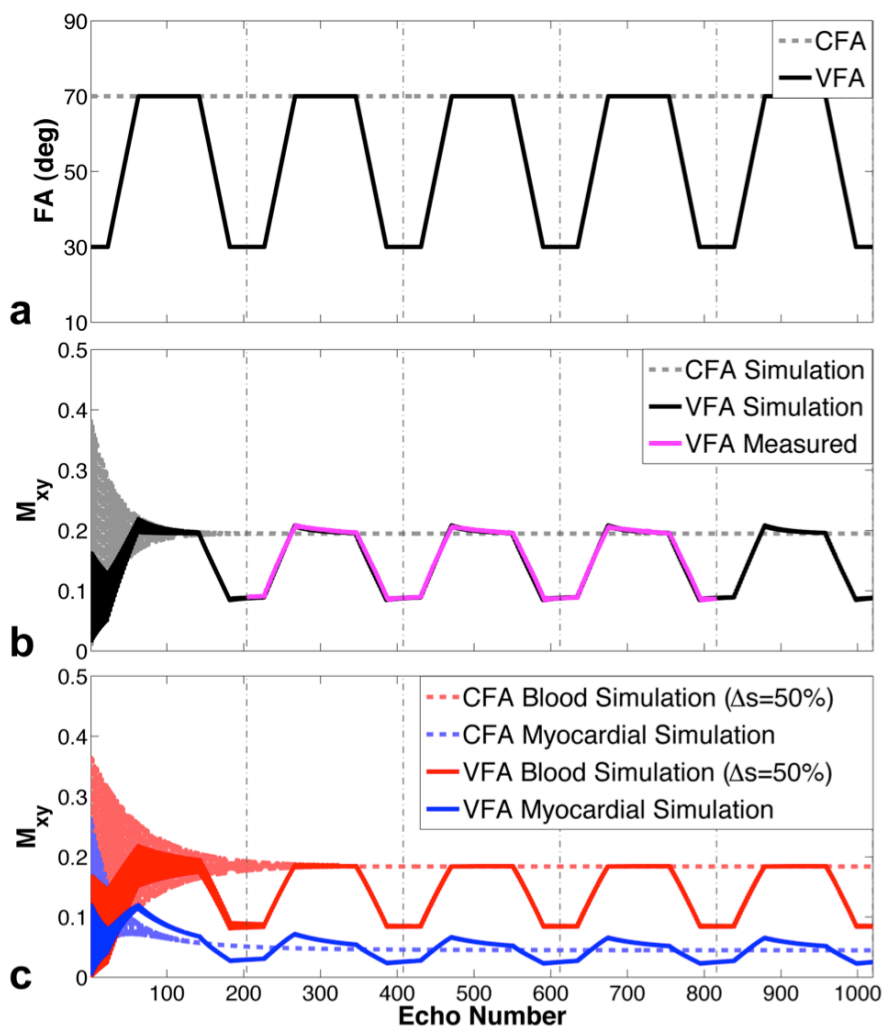


Figure 6.3: (A) The FA scheme for the CFA-bSSFP (70°) and VFA-bSSFP (30_70_40_80). The measured and simulated (B) transverse magnetization (phantom

$T_1/T_2=100/100\text{ms}$) for the CFA-bSSFP (dashed line) and VFA-bSSFP (solid line) schemes are shown. The simulations and measurements confirm that after ~ 150 echoes CFA-bSSFP transverse magnetization reaches a steady-state, whereas VFA-bSSFP transverse magnetization results in a dynamic steady-state. In (C) simulations of stationary myocardium ($T_1/T_2:867/57\text{ ms}$) and flowing blood ($T_1/T_2:1200/200\text{ ms}$, $\Delta s: 50\%$) for both CFA-bSSFP and VFA-bSSFP are shown.

Dynamic steady state (third shot) resolution phantom images (Fig. 6.4a-d) show that both the VFA-bSSFP and CFA-bSSFP schemes have similar sharpness for low-resolution objects (Fig. 6.4e). However, the smaller objects appear slightly blurred for VFA-bSSFP (30_70_40_80) compared to CFA-bSSFP (70°) due to the modulation of signal across k-space (Fig. 6.4f). SAR, however, is also decreased by 36% (0.49 vs. 0.76 W/kg). The simulation results show that the FWHM is increased 30% for the VFA-bSSFP scheme compared to CFA-bSSFP (1.3 vs. 1.0) as shown in Fig. 6.5a. The simulation of the FWHM of the point spread function and phantom measurements of the mean image blurriness measured from the line profile (Fig. 6.5c) along the phase encoding direction (Fig. 6.5a-b) agree well ($R = 0.91$) for the 25 different VFA-bSSFP experiments. Example images showing the simulated PSF of 70° CFA-bSSFP and 30_70_40_80 VFA-bSSFP are shown (Fig. 6.5e) and the line profiles drawn in the phantom images are also shown (Fig. 6.5f) for the corresponding acquisitions.

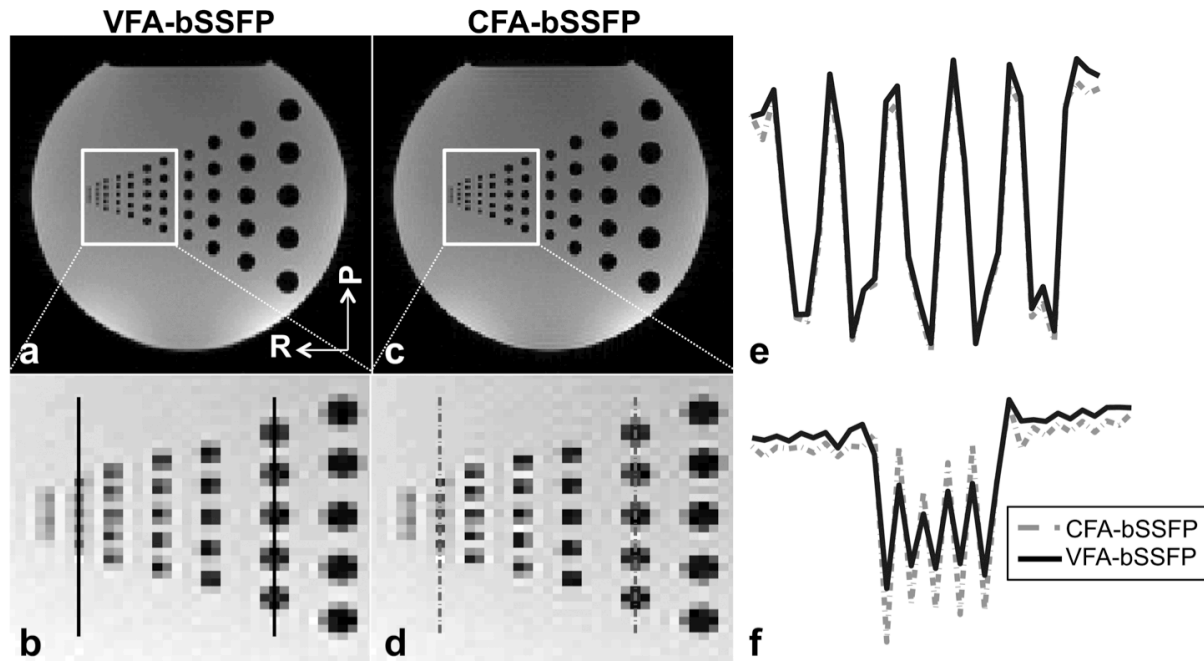


Figure 6.4: Dynamic steady state resolution phantom images acquired with 30_70_40_80 VFA-bSSFP (a) scheme and CFA-bSSFP of 70°(c). The corresponding zoomed images are shown in (b) and (d) with line profiles drawn over the sixth (e) and second (f) row (from left to right) of the resolution phantom for VFA-bSSFP (black solid line) and CFA-bSSFP (gray dashed line). The phase encoding (P) and the readout (R) axes are labeled.

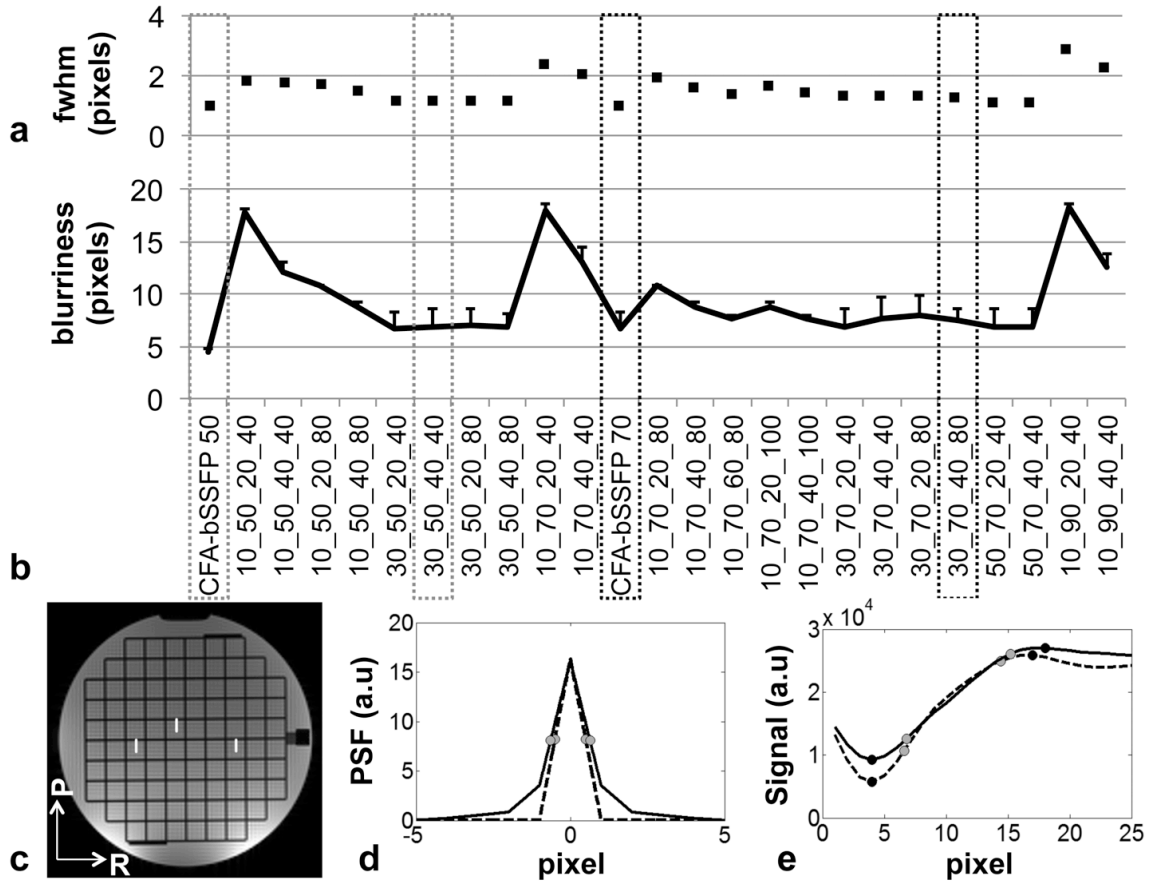


Figure 6.5: Simulated FWHM of the point spread function (a) and the mean of the measured image blurriness (b) over a line profile (c, solid white line) of the phantom along the phase encoding direction agrees well for the 25 different experiments. The phase encoding (P) and the readout (R) axes are labeled. The black dotted rectangles highlight the comparison of the CFA-bSSFP 70° with its corresponding 30_70_40_80 VFA-bSSFP scheme. The gray dotted rectangles highlight the comparison of CFA-bSSFP 50° and its corresponding 30_50_40_40 VFA-bSSFP scheme. Example simulations of the point spread function of CFA-bSSFP 70° (dashed line) and 30_70_40_80 VFA-bSSFP (solid line) are shown in (d) and the corresponding line profile drawn over the center solid line are shown in (e).

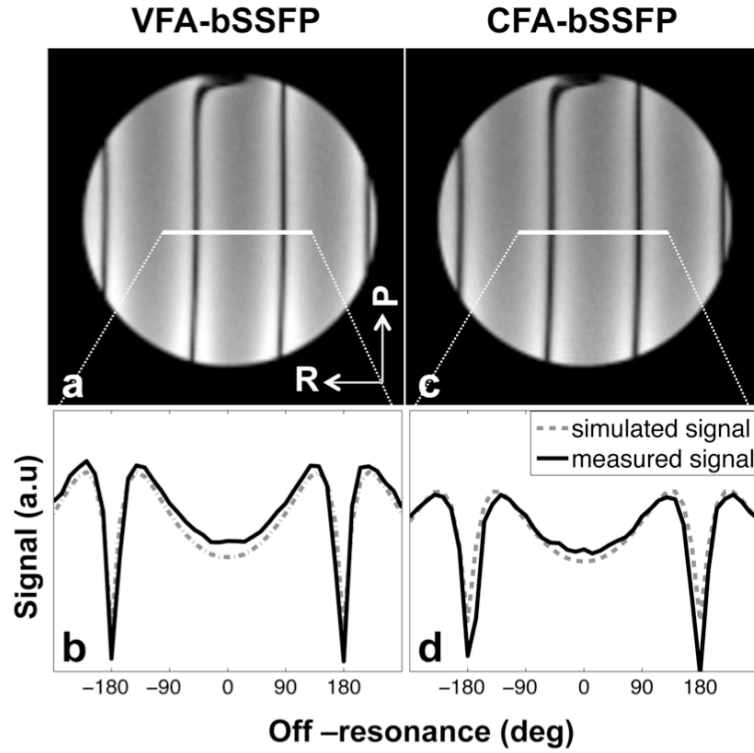


Figure 6.6: Phantom images acquired with an additional gradient of $200\mu\text{T/m}$ along the readout direction for 30_70_40_80 VFA-bSSFP (a) scheme and CFA-bSSFP of 70° (c). Simulated frequency profiles (solid line) and measured line profiles (dashed line) are shown for VFA-bSSFP (b) and CFA-bSSFP (d). The phase encoding (P) and the readout (R) axes are labeled.

The phantom experiments during application of the additional linear gradient shows that the VFA-bSSFP scheme has banding artifacts at multiples of $1/\text{TR}$ similar to the CFA-bSSFP scheme (Fig. 6.6a, c). The measured line profile and simulated frequency profiles (Fig. 6.6b, d) agree well ($R = 0.93$).

In Vivo Analysis

Diastolic and systolic images from the cardiac cines acquired in a normal subject with sCFA-bSSFP (FA=70°), aCFA-bSSFP of 70° and aVFA-bSSFP (30_70_40_80) are shown in Fig. 6.7. The SAR of aVFA-bSSFP compared to aCFA-bSSFP is significantly decreased by 36% (1.9 ± 0.2 vs. 3.0 ± 0.2 W/kg, $P < 10^{-10}$) for similar blood-myocardium CNR in the end diastolic phase (34 ± 6 vs. 35 ± 9 , $P = 0.5$). The SAR and blood-myocardium CNR of the sCFA-bSSFP were similar to aCFA-bSSFP experiments (3.0 ± 0.3 W/kg, 35 ± 7). Fig. 6.8 shows diastolic and systolic images acquired in a normal subject using the maximum (SAR limited) aCFA-bSSFP of 70° and aVFA-bSSFP (50_98_40_40). The blood-myocardium CNR of the aVFA-bSSFP compared to aCFA-bSSFP is improved by 28% (49 ± 9 vs. 38 ± 8 , $P < 10^{-4}$) with similar SAR (3.2 ± 0.5 vs. 3.3 ± 0.5 W/kg, $P = 0.6$).

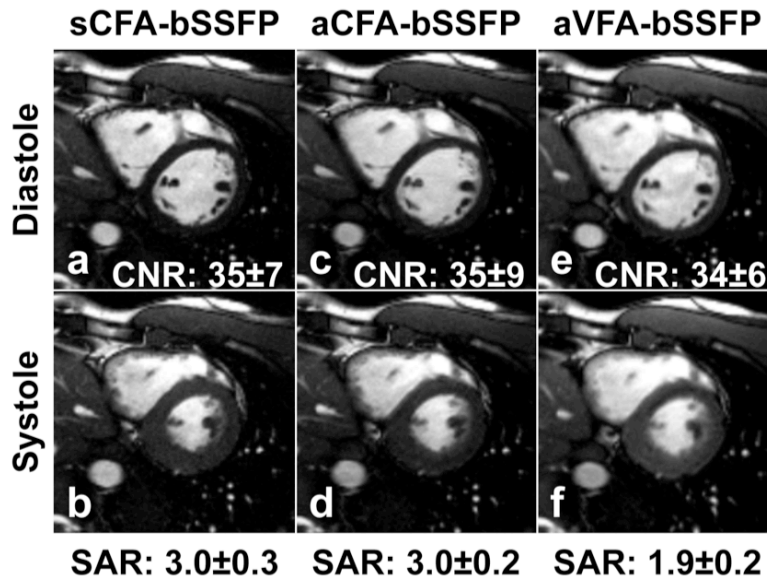


Figure 6.7: Diastolic (top row) and systolic (bottom row) images of a volunteer acquired with conventional sCFA-bSSFP (a-b) of 70°, aCFA-bSSFP (c-d) of 70° and 30_70_40_80 aVFA-bSSFP (e-f) scheme. aVFA-bSSFP has blood-myocardium CNR similar to aCFA-bSSFP (34 ± 6 vs. 35 ± 9 , $P = 0.5$) with reduced SAR (1.9 ± 0.2 vs. 3.0 ± 0.2

W/kg, $P < 10^{-10}$). The SAR and CNR of the sCFA-bSSFP were similar to aCFA-bSSFP experiments (3.0 ± 0.3 W/kg, 35 ± 7).

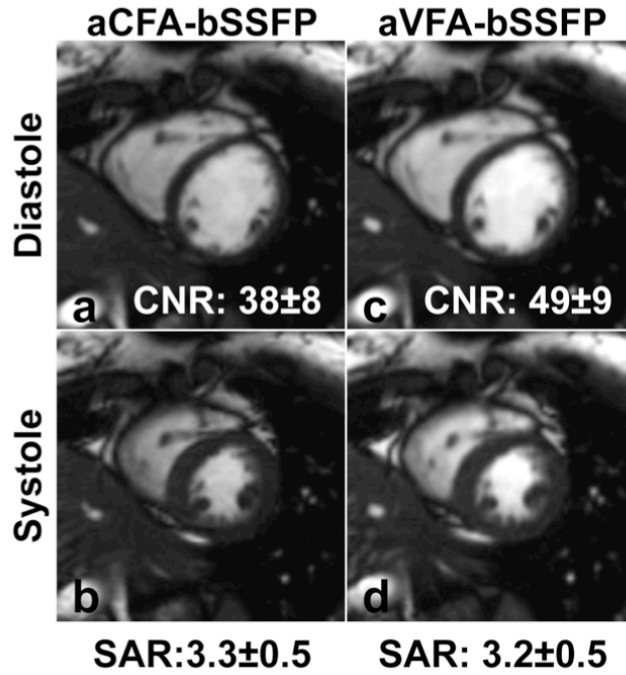


Figure 6.8: Diastolic (top row) and systolic (bottom row) images of a volunteer acquired with aCFA-bSSFP (a-b) of 70° and $50_98_40_40$ aVFA-bSSFP (c-d) scheme. aVFA-bSSFP has improved blood-myocardium CNR compared to aCFA-bSSFP (49 ± 9 vs. 38 ± 8 , $P < 10^{-4}$) with similar SAR (3.2 ± 0.5 vs. 3.3 ± 0.5 W/kg, $P = 0.6$).

Fig. 6.9 compares the simulated myocardial signal and the simulated flowing blood signals to the in vivo mean myocardial SNR and blood SNR in 10 subjects for the 25 different aVFA-bSSFP and aCFA-bSSFP experiments. The error bars show the standard deviation of these values in 10 volunteers. The mean and standard deviation of the SAR of each of these sequences is also indicated. The simulated signal and measured SNR of the myocardium ($R = 0.95$) and blood ($R = 0.98$) agree well.

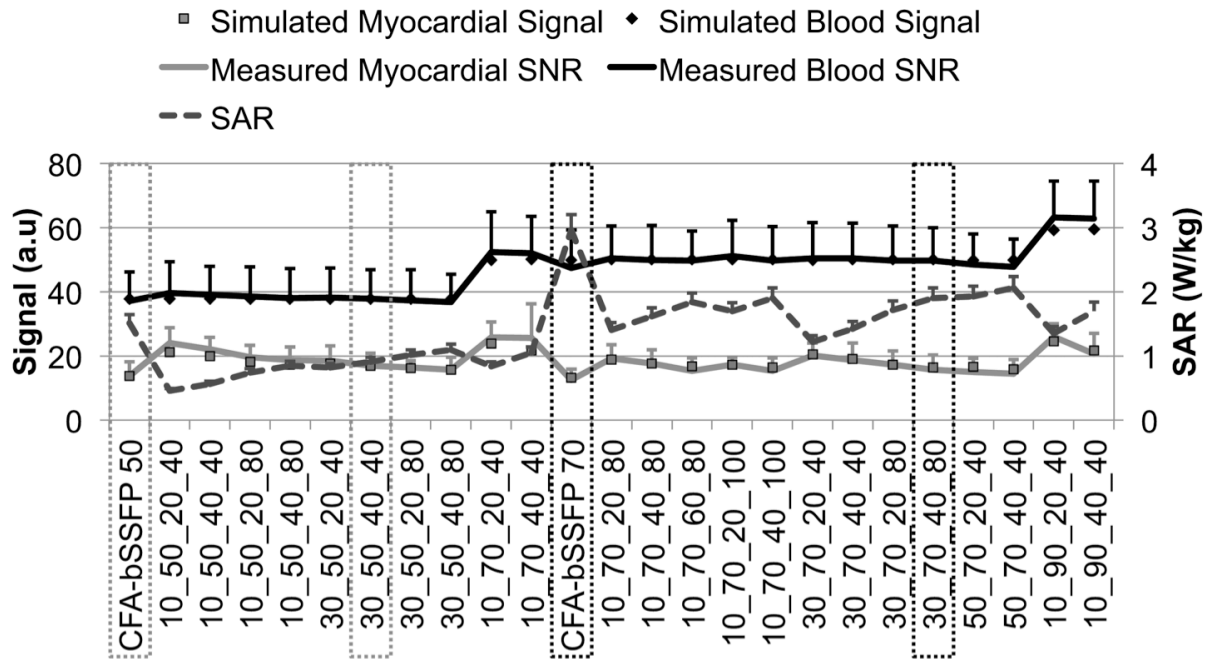


Figure 6.9: Measured myocardial (gray solid line) and blood (black solid line) SNR from diastolic images for 25 different aCFA-bSSFP and aVFA-bSSFP sequences agrees well with the simulated stationary myocardial (gray squares) and flowing blood (black diamonds). The SAR (dashed line) for each sequence is also shown.

6.10 DISCUSSION

aVFA-bSSFP can be used for low SAR cardiac cine imaging with similar myocardial and blood SNR and blood-myocardium CNR compared to the conventional sCFA-bSSFP sequence with minimal loss in image resolution. This may prove especially useful for imaging exams wherein SAR is a concern (patients with implanted devices and real time imaging). aVFA-bSSFP can also be used to improve the blood-myocardium CNR compared to the CFA-bSSFP with similar SAR because it accommodates a higher effective FA. This may prove especially useful for

cardiac cine imaging at 3T where the FA is typically SAR-limited, which results in lower than desired CNR; or facilitate higher CNR at 1.5T for more easier analysis of cardiac function.

Bloch simulations and the in vivo results show that aVFA-bSSFP can produce myocardial and blood signal similar to aCFA-bSSFP imaging while significantly reducing SAR and only slightly broadening the FWHM. The myocardial and blood signal simulations and in vivo myocardial and blood SNR results agree well. The current aVFA-bSSFP sequence does not accommodate parallel imaging, but the principles described herein are compatible with parallel imaging. When using parallel imaging the percent SAR reduction accorded by using aVFA-bSSFP will be less than when we don't use parallel imaging.

The different parameters for the aVFA-bSSFP scheme should be chosen carefully for cardiac cine imaging. The blood SNR of the aVFA-bSSFP scheme is strongly dependent on α_{high} . For example, two different VFA schemes with constant α_{high} , but variable N_{high} , N_{ramp} , and α_{low} such as 10_70_40_100 and 30_70_20_80 (Fig. 6.9) have similar ventricular blood SNR due to the strong dependence on α_{high} . Hence, α_{high} should be chosen based on the desired blood-myocardium CNR (higher α_{high} produces greater CNR).

Lower N_{high} and lower N_{ramp} pulses with low α_{low} reduces the SAR, but increases the image blurriness (e.g. 10_70_20_40 vs. 10_70_40_80 Fig. 6.5a-b). Furthermore, if N_{ramp} is too low ghosting artifacts (67) will arise due to the residual signal oscillations during transition between the low and high steady states. Therefore image blurriness and ghosting artifacts determine the lower bound on the acceptable N_{ramp} and N_{high} . Non-linear ramp trajectories such as a Kaiser-Bessel trajectory (51) could also be used to reduce signal oscillations during the transition between steady states while ramping from α_{low} to α_{high} , but initial results (not shown) indicate only minimally observable differences for $N_{\text{ramp}} \geq 20$. The upper bound of the N_{ramp} and N_{high} depends on the desired SAR reduction and image blurriness. For example, two VFA schemes with different N_{high} and N_{ramp} such as 10_70_20_100 and 10_70_40_80 have similar blood-

myocardium CNR and similar phantom image blurriness, but increased SAR of 1.69 vs. 1.62 W/kg respectively.

Lower α_{low} increases the image blurriness, but decreases the total acquisition SAR. For example, the VFA schemes 10_70_20_40 and 30_70_20_40 have measured phantom image blurriness of 18.6 vs. 11.4, simulated FWHM of 2.4 vs. 1.32 and SAR of 0.21 vs. 0.32 W/kg respectively. Hence, α_{low} should be chosen carefully such that the image blurriness is within acceptable limits for the overall reduction in SAR. Our experiments were performed with constant $N_{ky}=204$. The dependence of the VFA scheme parameters on the image blurriness and SNR should be considered even for experiments with different phase resolution (N_{ky}). The aVFA-bSSFP cardiac cine imaging did not use preparation pulses to catalyze the sequence to steady state. However, preparation pulses like Kaiser Bessel (68) can be used to further reduce the preparation duration and overall SAR of the sequence.

The results from Figs. 9 and 5a show that the 30_50_40_40 aVFA-bSSFP scheme produces the least difference in blood-myocardium CNR compared to aCFA-bSSFP of 50° (21±6 vs. 23±5) with a minimal increase in the FWHM to 1.2 and SAR reduced by 40% (0.9±0.1 vs. 1.5±0.1 W/kg). The 30_70_40_80 aVFA-bSSFP scheme produces the least difference in blood-myocardium CNR compared to aCFA-bSSFP of 70° (34±6 vs. 35±9) with minimal increase in FWHM to 1.3 and maximum reduction in SAR of 36% (1.9±0.2 vs. 3.0±0.2 W/kg).

Low SAR imaging is important in patients with implanted devices such as pacemakers and ICDs to reduce the heating at the lead tip that could damage the surrounding tissue (6). aVFA-bSSFP (30_70_40_80) can reduce the SAR by 36% compared to sCFA-bSSFP (70°) cardiac cine imaging, while maintaining SNR and CNR and largely preserving resolution. Further simulation and experiments need to be performed to optimize the aVFA-bSSFP scheme parameters to produce blood-myocardium CNR similar to sCFA-bSSFP while maximizing SAR reduction and minimizing image blurring.

6.11 Limitations

The aVFA-bSSFP sequence uses an asynchronous k-space acquisition. The asynchronicity provides acquisition of all k_y -lines during all cardiac phases. For example, if the $TR=4\text{ms}$, $N_{ky}=180$ ($TR \cdot N_{ky}=720\text{ms}$) and $RR\text{-interval}=800\text{ms}$, 10 cardiac phases can be acquired uniformly in 9 RR-intervals. If, however, $TR=4\text{ms}$, $N_{ky}=200$ ($TR \cdot N_{ky}=800\text{ms}$) and $RR\text{-interval}=800\text{ms}$, then the k-space acquisition and cardiac cycle are synchronous and the same k-space line will be acquired for each point in the cardiac cycle. Hence, only one cardiac phase can be reconstructed. This is also equivalent to acquiring synchronously the same single shot image for each cardiac cycle. However, in practice due to changes in the RR-interval during image acquisition, each cardiac phase may not be sampled uniformly. As a result, certain cardiac phases may be oversampled and the other cardiac phases may be under-sampled. Further developments and experiments are needed to refine techniques to uniformly sample k-space for all the cardiac phases.

The image blurriness was measured in the phantom images using the line profile along the phase encoding direction. These measurements agreed well with the simulation measurements of the FWHM of the point spread function (Fig. 6.5). However, similar measurements such as septal sharpness (66) over diastolic images did not result in significant differences between the aVFA-bSSFP and aCFA-bSSFP schemes due to poor alignment of the myocardial septum with the phase encoding direction and other concomitant sources of blurring.

6.12 CONCLUSIONS

aVFA-bSSFP can be used for: 1) low SAR (at least 36% lower) cardiac cine imaging with similar blood-myocardium CNR compared to the conventional sCFA-bSSFP imaging; or 2) high CNR (at least 28% higher) cardiac cine imaging with similar SAR compared to aCFA-bSSFP imaging, while nearly maintaining spatial resolution. aVFA-bSSFP may prove useful for cardiac structural

and functional imaging in patients with implanted devices, three-dimensional imaging, real time imaging, high-field imaging, and any cardiac cine application that is SAR-limited.

CHAPTER 7

FREE BREATHING VARIABLE FLIP ANGLE BALANCED SSFP CARDIAC CINE IMAGING AT 3T

Standard breath-hold cardiac cine imaging for conscious pediatric patients and patients with respiratory and/or cardiac dysfunction is challenging due to the need for repeated and reproducible breath holds. On the other hand, free-breathing acquisitions with bSSFP result in increased RF energy deposition due to their prolonged acquisition duration. In this work, we have used a variable flip angle approach similar to the technique used in Chapter 6, to lower the SAR and is acquired in free-breathing (FB-VFA), to overcome these challenges. The FB-VFA images were combined and reconstructed into cardiac cine images based on the recorded ECG timestamp and bellows signal and compared to the conventional breath-hold (BH-CFA) acquisitions. *The FB-VFA technique can be used to decrease the SAR of a free breathing cardiac cine imaging exam at 3T by 25-35% with image quality sufficient to perform global and regional cardiac function analysis.* This work, titled “Free Breathing low SAR Cardiac Cine Balanced SSFP Imaging at 3T” is in preparation for journal submission.

7.1 INTRODUCTION

The evaluation of cardiac function with standard breath-held MRI for conscious pediatric patients poses several challenges. Amongst them are the challenges of a multi-breath hold examination and the need to more carefully monitor the radiofrequency (RF) induced heating for patients that can have a heightened sensitivity to heating. Free breathing cardiac cine exams can be performed to reduce the need for multiple breath-hold exams. However, the free breathing acquisitions take longer to acquire compared to breath-hold acquisitions resulting in sustained RF induced heating causing increased patient discomfort. We sought to overcome

these two challenges by developing and evaluating a free-breathing cardiac cine bSSFP imaging exam at 3T that uses an optimized variable flip angle scheme (45,54) to lower the specific absorption rate (SAR) and real-time acquired cardiac cine images with bellows gated (30,69) respiratory motion correction to alleviate the need for breath holding.

Conventional cardiac cine imaging is routinely performed as an electrocardiogram (ECG) gated, k-space segmented, breath-hold imaging exam using bSSFP. Cardiac cine imaging is particularly well suited to bSSFP imaging due to its high signal-to-noise ratio (SNR) efficiency and high blood-myocardium contrast (70). Cardiac imaging benefits from increased SNR at 3T. bSSFP at 3T, however, presents additional challenges.

bSSFP is especially sensitive to the resonance frequency and banding and flow artifacts occur at off-resonance frequencies equivalent to multiples of the inverse of the repetition time (TR) (22,23). These artifacts are more pronounced at 3T due to increased B_0 inhomogeneities. These banding artifacts can be reduced by shortening the TR, shimming the field surrounding the heart to reduce the B_0 inhomogeneities (33), and by using frequency scout experiments (14) to select the imaging frequency that moves the bands outside the heart and flowing vessels. This approach works quite well for most patients at 3T.

Therefore, the first major limitation of breath-held cardiac cine bSSFP imaging is the need to repeatedly and reproducibly breath hold, which can be especially challenging for young pediatric patients and patients with respiratory and/or cardiac dysfunction. The artifacts that arise from poor breath holding will result in motion artifacts that complicate ventricular functional analysis.

The second major limitation of cardiac cine bSSFP imaging at 3T is the increased SAR, which arises due to the use of high imaging flip angles that are required for high blood-myocardium contrast (23,71). Recently, however, a variable flip angle (VFA) approach for cardiac cine imaging has been described, which can reduce the SAR while maintaining image quality (45).

Free-breathing cardiac cine imaging can be performed to reduce image artifacts due to poor breath-holding and simultaneously improve patient comfort. Numerous methods for respiratory motion compensation have been developed. Respiratory motion compensation can be performed using navigator echoes (72), but the application of the navigator echoes limits capturing the entire cardiac cycle and can disrupt the steady-state of the bSSFP signal leading to image artifacts. Herein we have adopted the approach of Kellman et al. (65) and acquired the images continuously in real-time, then retrospectively binned and reconstructed conventional cine images while reducing the SAR with a VFA approach.

METHODS

7.2 Choice of Optimal Variable Flip Angle Scheme

A previously reported VFA approach was adapted herein to lower the SAR of the acquisition without significantly altering the blood myocardium contrast (45). The symmetric trapezoidal VFA scheme had a number of flip angles equal to the number of phase-encoding lines. A number of α_{low} pulses (N_{low}) were used to acquire the outer k-space lines. The flip angle was linearly ramped up from α_{low} to α_{high} using N_{ramp} pulses (17) to smoothly increase the signal with reduced signal oscillations. The center k-space lines were acquired using α_{high} with increased signal and ramped down back again to α_{low} . The parameters of the VFA scheme that maximizes the deposited RF energy reduction while maintaining the blood-myocardium contrast and point spread function (PSF) similar to a conventional constant flip angle k-space segmented acquisition scheme was determined using Bloch simulations performed in MATLAB (The Mathworks, Natick, MA, USA).

Signal simulations of stationary myocardium ($T_1/T_2=1471/47$ ms) and flowing blood ($T_1/T_2/T_2^*=1932/275/138$ ms) (43) at 3T were performed with the following parameters: TR = 2.8ms, echo time (TE) = 1.4ms, 93 RF pulses per measurement (N_{ky}), and 10 consecutive shots (measurements). The spin density (M_0) of the myocardium and blood was $M_{0\text{myo}}=0.7$ and

$M_{\text{blood}}=0.95$ (33). An imperfect slice profile (42) was simulated using a windowed sinc RF pulse with time bandwidth product of two for 20 sub-slices (N_s). The resultant flip angle within each sub-slice was determined using the inverse sine of the slice profile. The simulations accounted for flowing blood similar to Markl et al. (22,23) by replacing 50% of the spins within the imaging slice per TR (Δs) and tracking the magnetization for a number of out-of-slice sub-slices (N_{os}) equivalent to $N_{os}=5 \times \Delta s \times N_s \times T_2^*/TR$. This effectively tracks spins outside the imaging slice until the signal is decayed by T_2^* effects.

The signal simulations were repeated for every combination of N_{ramp} between 20 to 45 in steps of five pulses, N_{low} between zero to 25 in steps of five pulses, $\alpha_{\text{low}} = 5^\circ$ to 40° in steps of 5° and $\alpha_{\text{high}} = [40^\circ, 50^\circ]$. As not all combinations are realizable, any combination of VFA scheme with negative $N_{\text{high}} = N_{\text{ky}} - (2 \times N_{\text{ramp}} + 2 \times N_{\text{low}})$ was not simulated. The blood-myocardium contrast was calculated as the signal difference between flowing blood signal and stationary myocardium signal measured from the central echo of the last measurement. The deposited RF energy by each of these VFA schemes was estimated as the sum of squares of individual flip angles of the VFA scheme. The point-spread function of each VFA scheme was calculated from the Fourier transform of the last shot. The full width half max (FWHM) of the PSF was measured as the width of the PSF at half the maximum value to estimate the resolution loss due to the k-space weighting introduced by each VFA scheme. The blood-myocardium contrast and deposited RF energy were also calculated for simulations with constant flip angle (CFA) of 40° .

The final optimal VFA scheme was chosen by selecting a sub-set of these VFA schemes with contrast greater than or equal to the contrast of CFA = 40° , with RF energy deposited lesser than the CFA = 40° and FWHM less than or equal to 1.2 were chosen. Among these, the VFA scheme with the least SAR was chosen as the optimal VFA scheme.

7.3 Bellows gated VFA Imaging Acquisition and Reconstruction

The different steps used in the reconstruction of FB-VFA cardiac cine images are explained in Fig. 7.1. Respiratory motion compensation for free-breathing cardiac cine imaging was performed retrospectively using bellows gating. The VFA cardiac images were continuously acquired to maintain the dynamic steady state signal. The bellows signal and the electrocardiogram (ECG) timestamp from the QRS trigger were recorded during the acquisition of each k_y line. The RR interval variations were adjusted by normalizing the ECG timestamp. The respiratory gating window was chosen by setting a patient specific threshold on the bellows signal (25% to 35%). The k-space lines within the respiratory gating window were sorted based on their normalized ECG timestamp and linearly interpolated in time into the desired number of cardiac phases individually for each coil. This reconstruction was implemented on the Siemens scanner and the data was further processed for GRAPPA reconstruction (73) and final image reconstruction.

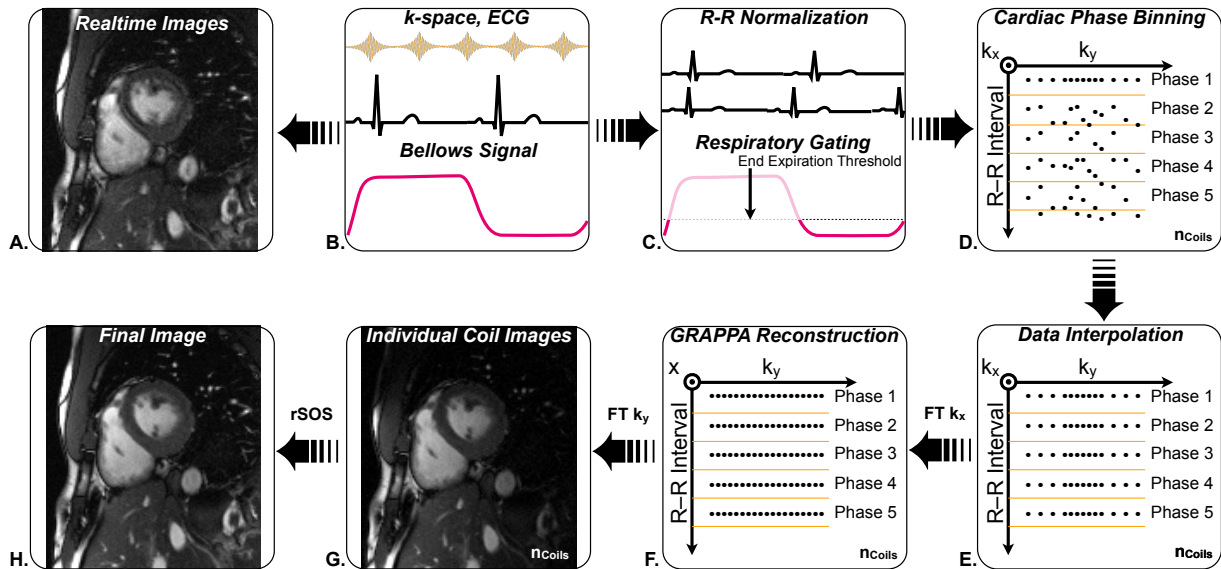


Figure 7.1: The cardiac cine reconstruction scheme of free-breathing, bellows gated, variable flip angle acquisition. The ECG and the bellows signal are noted during

acquisition of each k_y -line (B). The RR interval is normalized to account for RR interval variation and the k_y lines not within the gating window are discarded. Each k_y line is sorted based on the ECG timestamp (D) and are linearly interpolated into number of desired cardiac phases (E). The data is Fourier transformed (FT) in k_x direction and GRAPPA reconstruction is used to fill the missing k_y lines (F). The individual coil data (G) are combined for each cardiac phase to form the final cardiac cine images (H).

7.4 In Vivo Imaging Experiments

All images were acquired on a 3T scanner (Trio; Siemens Medical Solutions, Erlangen, Germany) using a 6-channel anterior cardiac coil and 6-channel posterior spine matrix.

Cardiac exam were performed in 10 healthy subjects (N=10, 9 male, age= 29 ± 5 years) subsequent to obtaining informed written consent using an IRB approved protocol. Conventional two dimensional, multi-slice, retrospectively cardiac gated, breath-hold, short-axis CFA (BH-CFA) bSSFP images were acquired covering the whole left ventricle (LV) from the apex to the base. Single slice, four chamber, long-axis bSSFP images were also acquired using BH-CFA.

The imaging parameters for BH-CFA and FB-VFA were: FOV= 360×303 mm, slice thickness= 6mm, slice gap= 4mm, 10 to 12 slices, imaging resolution = 1.9×1.9 mm, TR/TE = 2.8/1.4 ms, bandwidth= 1371 Hz/px, using the maximum SAR-limited flip angle= $38.5^\circ \pm 2.4^\circ$, k_y lines per segment=12, reconstructed cardiac phases=20, with GRAPPA factor of two and 24 reference lines. The acquisition duration was 8 ± 1 seconds per slice. Patient specific frequency scouts (14) were performed for different slices to choose the imaging frequency with least artifacts within the left ventricle. Each slice was acquired at the iso-center with patient-specific local cardiac shimming to reduce B_0 inhomogeneities.

In addition, multi-slice, short-axis, free-breathing, bellows-gated VFA (FB-VFA), cardiac images, optimized for low SAR imaging were acquired with identical acquisition parameters.

Single slice FB-VFA images were also acquired in four chamber long-axis view at the same location as BH-CFA. The individual VFA images had a temporal footprint of 263ms and were acquired continuously for one minute ($N_{\text{shots}}=228$).

7.5 Qualitative Image Analysis

The image quality of the mid-ventricular short-axis and four chamber long-axis slices of the BH-CFA and FB-VFA acquisition were scored independently by two radiological experts. At the time of image evaluation both experts were blinded to the aim of the study and the differences between the image acquisition methods. Cines for a single mid-ventricular short-axis slice and a single long-axis slice for all subjects were displayed blinded to the acquisition scheme in a randomized manner and were scored using a 5-point scale with increments of 0.5 similar to Kellman et al. (65) and Hansen et al. (74) with 5 being excellent. A score of 5 indicated that the reconstruction had good blood-myocardium contrast with fine structural details readily apparent, did not have artifacts, and regional and global cardiac function were easily assessable. A score of 4 indicated that there was acceptable blood-myocardium contrast and insignificant artifacts with adequate image quality to determine global and regional cardiac function. A score of 3 was given to images with fair image quality that could be used to evaluate global and regional cardiac function, but image contrast and/or image artifacts were notable. A score of 2 was given to images where blood-myocardium contrast was poor artifacts were significant, and/or regional function could not be determined. A score of 1 indicated non-diagnostic image quality for evaluating even global cardiac function. Statistical differences between the two techniques and between the observers were evaluated using paired, Student t-test with $P < 0.05$. The t-test values were Holm-Sidak post-hoc corrected.

Lastly, both the experts analyzed the presence or absence of slice mis-registration in the breath-hold and free breathing data by re-formatting the diastolic multi-slice short-axis images. The qualitative analysis was performed in using Osirix (<http://www.osirix-viewer.com/>).

7.6 Quantitative Image Analysis

The left ventricular ejection fraction (LVEF), end diastolic volume (LVEDV), end systolic volume (LVESV), stroke volume (LVSV), and end diastolic myocardial mass (LVEDM) were determined by manual contour analysis using commercial software (Argus, Siemens, Medical Systems, Erlangen, Germany) for both BH-CFA and FB-VFA acquisitions. The contouring was performed by experienced MR technologists with over 10 years of experience contouring clinical cases. The same MR technologist contoured for each subject's BH-CFA and FB-VFA exam, but were otherwise blinded to the study. Statistical differences between the two techniques were evaluated using paired, Student t-test. The t-test values were Holm-Sidak post-hoc corrected.

The apparent SNR was measured in the LV blood, RV blood, and myocardial septum in both end diastolic and end systolic cardiac phases in the mid-ventricular short-axis slice using region-of-interest (ROI) analysis. The standard deviation of the noise was determined from an ROI drawn in the background region. The apparent SNR was divided by a correction factor (4) of

$\sqrt{\frac{2}{4-\pi}} = 1.53$, to account for the Rayleigh distribution of the noise. Contrast to noise ratio (CNR)

between the LV blood and myocardium was also evaluated. These apparent SNR measurements are a suitable method for comparing two acquisition strategies that have largely the same acquisition parameters even when parallel imaging is being used provided the acquisitions otherwise use identical imaging parameters. Statistical differences between the two techniques were evaluated using paired, Student t-test with $P < 0.05$. The t-test values were Holm-Sidak post-hoc corrected.

7.7 RESULTS

Fig.7.2 shows the Bloch simulation results of the maximum FWHM chosen from the blood and myocardial tissue signals, the deposited RF energy (sum of squares of the flip angles in the VFA scheme) as a surrogate for SAR, and contrast between flowing blood ($\Delta s=50\%$) and

stationary myocardial signal. The optimal VFA scheme was $\alpha_{\text{high}} = 50^\circ$, $\alpha_{\text{low}} = 25^\circ$, $N_{\text{low}} = 25$, $N_{\text{ramp}} = 20$ and $N_{\text{high}} = 93$. This VFA scheme resulted in 35% lower SAR than $\text{CFA} = 40^\circ$ with $\text{PSF} = 1.18$ with blood-myocardium contrast of 0.11 identical to $\text{CFA} = 40^\circ$. The simulated blood and myocardium signal for this VFA scheme, however, was higher at 0.18 and 0.07, respectively. Whereas for $\text{CFA} = 40^\circ$ the simulated blood signal was 0.15 and the myocardium signal was 0.04.

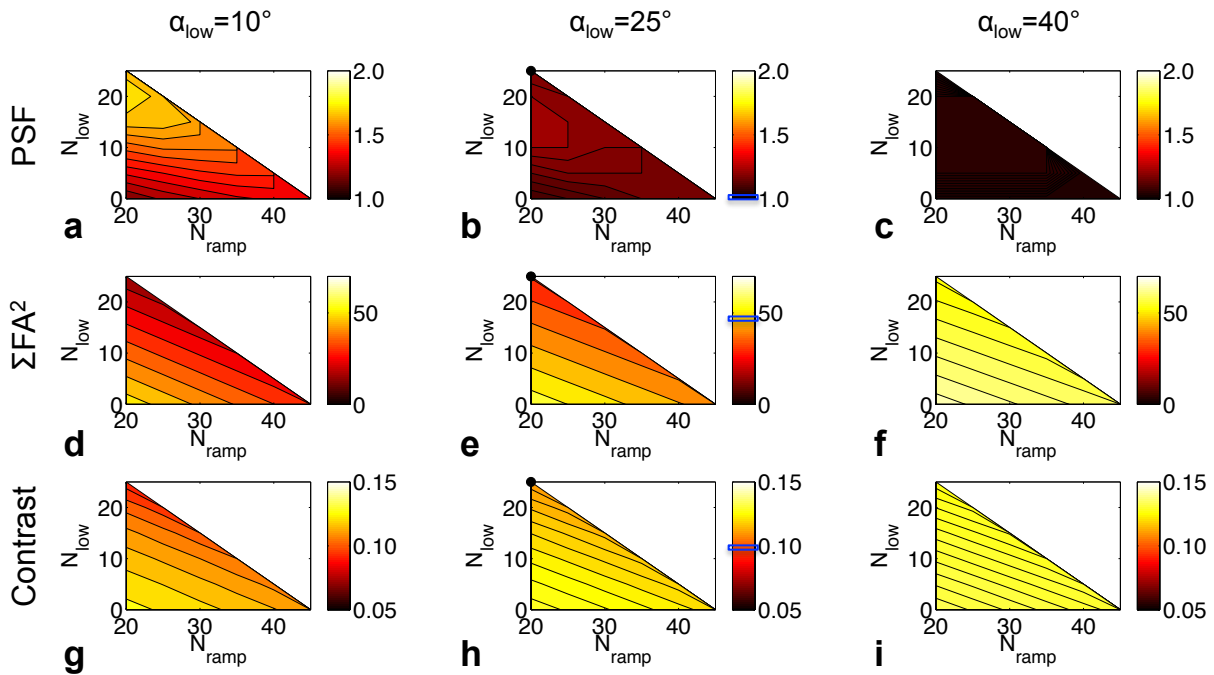


Figure 7.2: Bloch simulation of the point spread function (PSF) (a to c), sum of squares of the variable flip angle (VFA) scheme (d to f), and contrast between flowing blood and stationary myocardial signal (g to i) for varying number of ramp pulses (N_{ramp}) and number of low pulses (N_{low}) for $\alpha_{\text{low}} = 10^\circ$ (a,d,g), $\alpha_{\text{low}} = 25^\circ$ (b,e,h) and $\alpha_{\text{low}} = 40^\circ$ (c,f,i) with constant $\alpha_{\text{high}} = 50^\circ$ and $N_{\text{ky}} = 93$. The blood-myocardial simulation with constant flip angle (CFA) of 40° resulted in a point spread function of 1, with sum of flip angles = 45.33 rad^2 , and contrast = 0.11 as indicated in the color bars. The VFA scheme which produces the

least sum of squares of flip angle with contrast similar to CFA of 40° , with PSF of 1.18 is $N_{\text{low}}=25$, $N_{\text{ramp}}=20$, $\alpha_{\text{low}}=25^\circ$ and $\alpha_{\text{high}}=50^\circ$ as shown in black circles.

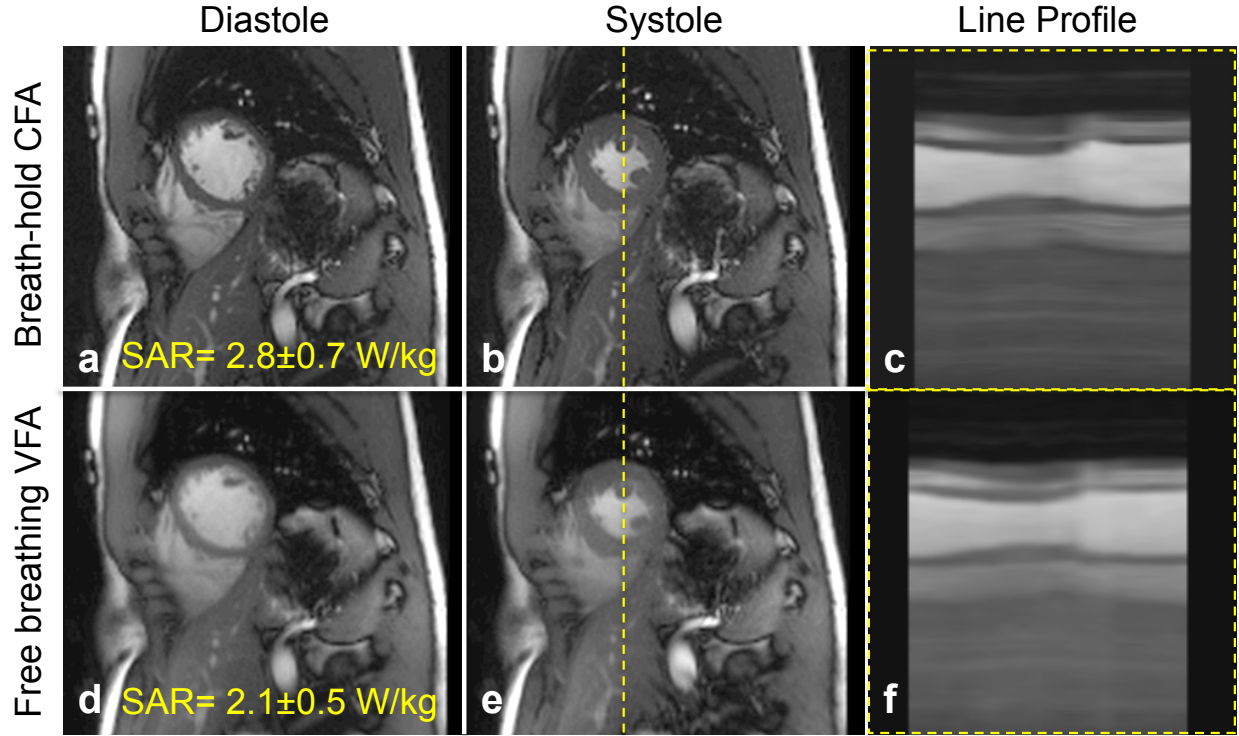


Figure 7.3: Diastolic and systolic mid-ventricular short-axis images acquired with breath-hold, constant flip angle (BH-CFA) acquisition (a,b) and reconstructed free-breathing, bellows-gated, variable flip angle (FB-VFA) acquisition (d,e). The line profile along the cardiac cine images are shown in c and f.

Fig.7.3 shows example mid-ventricular, short-axis, cardiac cine images acquired in a healthy subject during systolic and diastolic cardiac phases using both BH-CFA and FB-VFA acquisitions. The SAR is decreased by 25% using FB-VFA compared to BH-CFA. A line profile of the cardiac cine images shows the clear depiction of the blood-myocardium borders in each cardiac phase in the BH-VFA images that are comparable to the FB-CFA acquisition.

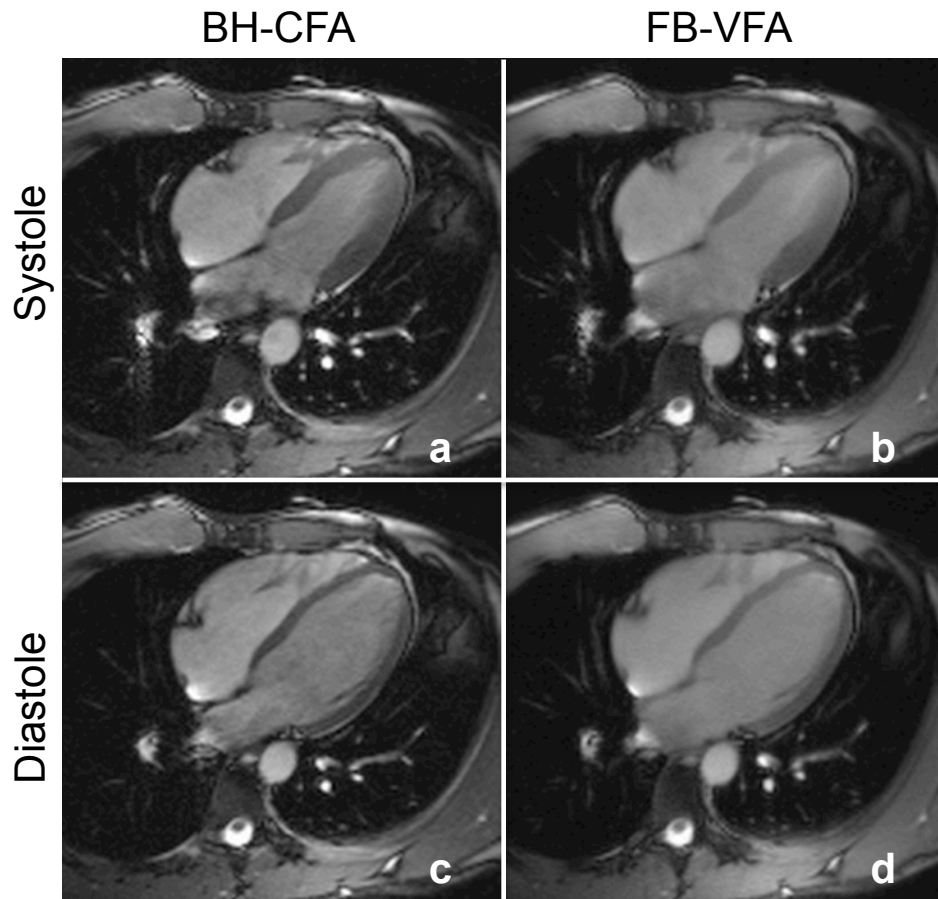


Figure 7.4: Four chamber systolic and diastolic cardiac images acquired with breath-hold, constant flip angle (BH-CFA) acquisition (a,c) compared to bellows-gated, variable flip angle (FB-VFA) cardiac cine images (b,e) showing clear depiction of the systolic phase comparable to the breath-hold acquisition.

An example four-chamber cardiac cine images comparing the BH-CFA and the FB-VFA cardiac cine images is shown in Fig.7.4. A single cardiac phase with a temporal resolution of 50ms was recovered well from the acquired images with a temporal resolution of 263 ms and an RR-interval of 1000ms.

The image quality score for both short-axis and four-chamber view images is shown in Table 7.1. The average score for the short-axis FB-VFA acquisition was significantly different than the BH-CFA acquisition (3.1 ± 0.5 vs. 4.3 ± 0.8 , $P < 0.05$). The average score for the four chamber long-axis FB-VFA acquisition was significantly different than the BH-CFA acquisition (3.4 ± 0.4 vs. 4.6 ± 0.6 , $P < 0.05$). Notably, the scores reported by both experts were within 0.5 point of each other for 82.5% of the cases and there were no significant differences between experts ($P > 0.05$).

	Short-axis		Long-axis	
	BH-CFA	FB-VFA	BH-CFA	FB-VFA
Observer-1	4.1±1.0	3.2±0.5*	4.7±0.6	3.4±0.5*
Observer-2	4.5±0.6	3.0±0.3*	4.6±0.6	3.4±0.4*

Table 7.1: The average image quality score in mid-ventricular short-axis and long-axis images. * indicates significant differences ($P < 0.05$).

	BH-CFA	FB-VFA
Ejection Fraction	60±6	63±4
End Diastolic Volume	128±23	134±21*
End Systolic Volume	51±9	49±7
Stroke Volume	77±19	86±17*
End Diastolic Myocardial Mass	95±23	93±23

Table 7.2: Left ventricular quantitative measurements from BH-CFA and FB-VFA acquisitions. * indicates significant differences ($P < 0.05$).

Both the experts observed that there was slice mis-registration in three out of ten subjects in BH-CFA. One of the experts observed that one additional BH-CFA and one additional FB-VFA were mis-registered.

Table 7.2 shows the mean LVEF, LVEDV, LVESV, LVSV, and LVEDM for FB-VFA and BH-CFA in 10 healthy subjects. The LVEDV and the LVSV were statistically different between BH-CFA and FB-VFA. The linear fit of LVEDV, LVESV and LVSV between BH-CFA (V_{CFA}) and FB-VFA (V_{VFA}) was $V_{VFA}=1.02 \cdot V_{CFA}+2.51$. The correlation coefficient (R) between the BH-CFA and FB-VFA volumes was 0.98.

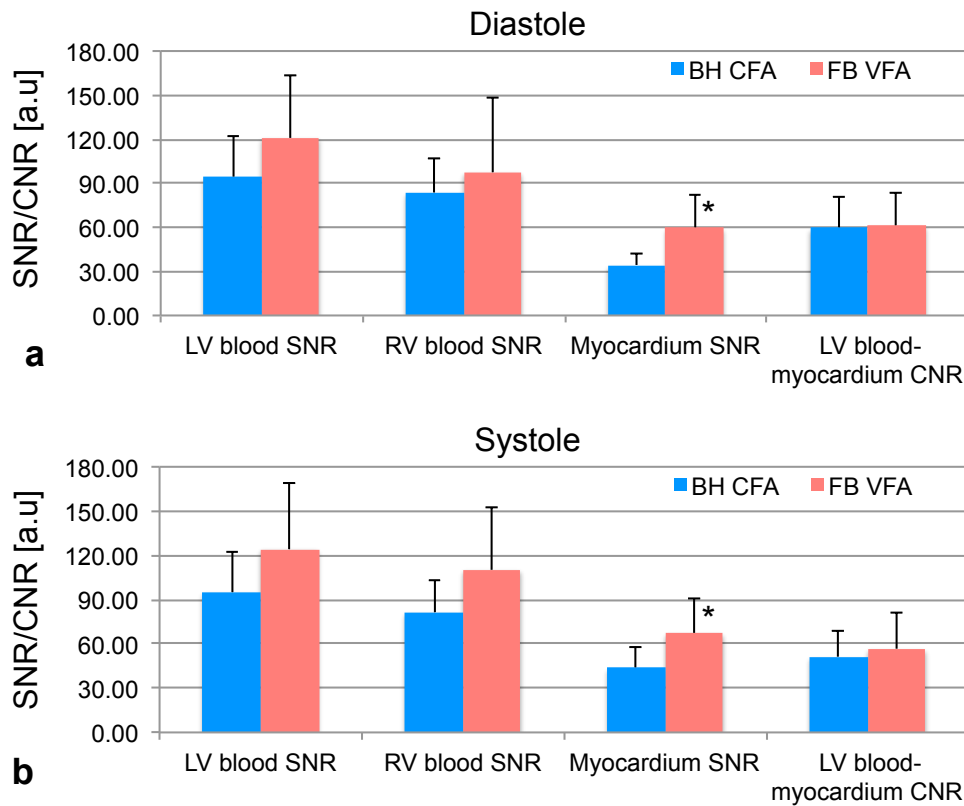


Figure 7.5: Signal to noise ratio of left ventricular (LV) blood, right ventricular (RV) blood, and myocardium and contrast to noise ratio (CNR) between the LV blood and myocardium measured in mid-ventricular short-axis slice in 10 healthy subjects at end diastole (a) and end systole (b). The SNR of LV blood, RV blood and myocardium are

higher using bellows-gated, variable flip angle (FB-VFA) compared to breath-hold, constant flip angle (BH-CFA) with myocardial SNR being significantly different. The CNR between LV blood and myocardium is similar for both BH-CFA and FB-VFA. * indicates $P < 0.05$.

Fig.7.5 shows the measured SNR of the LV blood, RV blood and myocardium and the blood-myocardium CNR for both BH-CFA and FB-VFA at end diastole and end systole. The measured SNR was higher in FB-VFA compared to BH-CFA for all the regions. However, only myocardial SNR was significantly different and higher for FB-VFA compared to BH-CFA. The LV blood-myocardial CNR was not significantly different between the two techniques.

7.8 DISCUSSION

VFA bSSFP can be used for free-breathing cardiac cine imaging with sufficient image quality for measuring global and regional cardiac function. CFA bSSFP at 40° on a 3T scanner produces high image contrast, but also approaches the SAR limit. Herein, Bloch equation simulations were used to determine the optimal VFA scheme for blood-myocardium contrast similar to CFA of 40° , while reducing the SAR and maintaining image resolution. The maximum myocardial signal occurs when the FA is in the range of 30° to 40° (71) at 3T. In general, the VFA scheme increases the SNR of the myocardium (54) and is not governed by α_{high} alone. The flowing blood signal, however, is approximately the same for the VFA and CFA schemes and largely governed by α_{high} (45). Hence, to maintain the blood-myocardium contrast, the flowing blood signal was increased by using $\alpha_{\text{high}}=50^\circ$ at the cost of increasing the PSF by 1.18.

The scanner reported SAR is calculated for different time intervals (i.e. 10 s, 90 s and 360 s). As the BH-CFA sequence was less than 10s in acquisition duration the average SAR of this sequence within 10s can be reduced by an enforced delay after the scan during which no

scanning can occur. However, this SAR reduction strategy is not feasible for FB-VFA with an acquisition duration of one minute. This may account for the discrepancy between the achievable 25% SAR reduction in in vivo experiments compared to the estimated 35% reduction of using Bloch simulations. The discrepancy was also due to the lower SAR limited FA of $38.5^{\circ} \pm 2.4^{\circ}$ used in in vivo imaging experiments compared to the simulated CFA of 40° used for estimation. The ability to use a higher α_{high} for FB-VFA can be used to improve the image contrast in cardiac cine acquisitions compared to FB-CFA acquisitions (72), which can be SAR limited at a lower α_{high} .

The real-time images were acquired with a temporal footprint of 263ms and were insufficient for evaluating global and regional cardiac function. Hence, ECG timestamp and bellows signal were used for cardiac and respiratory motion compensation of FB-VFA images. Image-based navigators (65,74) can also be used for retrospective respiratory motion compensation with a shorter temporal footprint for sufficient sampling of the respiratory motion. However, prospective motion compensation using image based navigators, to determine scan specific acquisition duration may be computationally expensive. Alternatively, bellows can be used for monitoring the k-space filling and prospectively determining the acquisition duration, and image based navigators can be used to retrospectively warp the images within the respiratory window for reduced respiratory motion artifacts. The acquisition duration can also be further reduced using compressed sensing (75-77).

FB-VFA was determined to be of slightly above fair quality compared to the BH-CFA acquisitions. The image quality scores of both BH-CFA and FB-VFA were lower than the quality scores presented in Hansen et al. This could be due to several reasons. Firstly, images in this study were acquired at 3T wherein flow and banding artifacts are more prevalent. The flow artifacts were more pronounced in FB-VFA compared to BH-CFA, due to respiratory induced movement of the excited slice and the resultant persistence of signal outside the desired slice until the signal decayed due to T_2^* effects. Frequency scouts were used to remove the banding

from the heart, but the bands were necessarily present in blood vessels farther from the heart and within the imaging FOV in both BH-CFA and FB-VFA. Secondly, the FWHM of the PSF for FB-VFA is broader than for BH-CFA, which resulted in image blurriness. Thirdly, the bellows signal was used for respiratory motion compensation and image-based motion fields were not used to directly estimate motion correction within the gating window. Lastly, it is difficult to control for intra-institute differences in scoring criteria.

The observed increase in LVEDV and decrease in LVSV for FB-VFA compared to BH-CFA accords with the expected differences in LV volumes obtained during free-breathing and breath held exams. Breath holding is known to increase intrathoracic pressure, which reduces pre-load and consequently LVEDV. The lower LVEDV leads to a lower stroke volume in accordance with the Frank-Starling effect. Hence, these differences likely reflect normal physiology.

Limitations

The RF pulse center frequency for the free-breathing acquisitions was set based on the RF pulse center frequency of the breath-hold acquisitions at the same imaging location. FB-VFA acquisitions, however, had more flow-related off-resonance artifacts compared to BH-CFA due to respiratory motion induced shifts in the field and subsequently off-resonance bands. This may be reduced in FB-VFA acquisitions by slowly varying the RF pulse frequency with respect to bellows signal, perhaps between two center frequencies chosen for best image quality at end inspiration and end expiration.

The FB-VFA images were acquired for a fixed duration of one minute and retrospectively reconstructed after thresholding of the bellows signal. The retrospective selection of the bellows gating threshold, however, could be automatically set during a scout exam that compares the diaphragm navigator and the bellows signal.

7.9 CONCLUSION

VFA bSSFP imaging can be used to decrease the SAR of a free breathing cardiac cine imaging exam at 3T with image quality sufficient to perform global and regional cardiac function analysis.

CHAPTER 8

FAST VARIABLE FLIP ANGLE 3D T_2 -TIDE PROSTATE IMAGING

Three dimensional (3D) T_2 weighted fast spin echo (FSE) anatomic imaging of the prostate currently requires long acquisition times resulting in patient discomfort as well as increased susceptibility to motion artifacts. The long acquisition duration using FSE imaging is due to the limited echo train duration of FSE sequences as well as the increased SAR due to high flip angle refocusing pulses. Our objective was to develop a fast 3D T_2 weighted bSSFP sequence for prostate imaging at 3T using a variable flip angle transition into driven equilibrium (T_2 -TIDE) scheme. Paul et al., have proposed a 2D T_2 weighted bSSFP imaging technique (Chapter 5.4). We have used a similar variable flip angle optimized for 3D imaging at 3T, with a spiral-out phase encode ordering for faster and efficient sampling of the k_y - k_z plane for T_2 weighted imaging. bSSFP imaging is used to increase the echo train duration compared to FSE imaging. Interleaved spiral-out phase encode ordering is used to improve the image sharpness. *The novel 3D T_2 -TIDE imaging technique can acquire T_2 weighted images ~58% faster than conventional 3D FSE with matched imaging parameters. The SNR efficiency of 3D T_2 -TIDE images is also improved compared to 3D FSE.* This work, titled “Fast Three-Dimensional T_2 -weighted Imaging with Transition Into Driven Equilibrium balanced SSFP at 3T” is in review for journal publication in Magnetic Resonance in Medicine. This work was also, in part, presented at ISMRM, Milan, 2014, abstract: 4120.

8.1 INTRODUCTION

T_2 weighted prostate MRI is the clinical standard for anatomic imaging of prostate (78) and is routinely performed using fast spin echo techniques (i.e FSE, TSE, or RARE). Three dimensional (3D) T_2 weighted prostate imaging is preferred for imaging small tumors and for

acquiring near isotropic slices that are amenable to multi-planar reformatting, which is useful for multi-modal registration applications during biopsy, surgical, or treatment planning (79).

The conventional 2D FSE sequences use a series of 180° refocusing pulses with a long repetition time for signal recovery to produce purely T_2 weighted images. The use of 180° pulses increases the specific absorption rate (SAR) of the sequence especially at 3T and the number of acceptable refocusing pulses is further limited due to fast signal decay and concomitant image blurring. These disadvantages can be overcome by designing variable flip angle (VFA) schemes that use refocusing flip angles (FA) $< 180^\circ$ for T_2 weighted FSE (50,52,80). However, three-dimensional T_2 weighted FSE prostate imaging, can take over 7 minutes to acquire even with a VFA scheme.

Balanced steady state free precession (bSSFP) imaging is widely used for numerous clinical applications due to its high signal to noise ratio (SNR) efficiency. However, the steady state signal of bSSFP is T_2/T_1 weighted, which is not desirable for clinical applications where the underlying abnormality may vary in both T_1 and T_2 . 2D single-shot T_2 weighted imaging has previously been demonstrated using SSFP techniques such as 2D T_2 -TIDE (55) and 2D T_2 VAPSIF (56) based on the transition into driven equilibrium (TIDE) sequence (17). In these approaches the T_2 weighted signal is obtained by acquiring the central k-space lines during the transient state of the SSFP magnetization using FA= 180° followed by ramping down the FA to a lower FA while acquiring the outer k-space lines, to reduce the overall SAR and maintain the sharpness of the reconstructed image. The T_2 contrast in these techniques is controlled by the initial number of 180° pulses and the partial Fourier factor, similar to 2D single-shot half-Fourier acquisition single-shot turbo spin-echo (HASTE) imaging (81). Extension of these techniques to 3D encoding schemes, however, is not practical because of the SAR limitation that arises from the long acquisition durations especially for short pulse repetition times (TR) at higher field strengths ($\geq 3T$).

Our objective was to overcome these limitations by developing and evaluating a novel method for fast 3D T_2 weighted TIDE (3D T_2 -TIDE) bSSFP imaging with application to prostate imaging at 3T. 3D T_2 -TIDE uses a VFA scheme similar to 2D T_2 -TIDE to reduce the SAR and maintain the T_2 contrast by acquiring the central k-space lines first during the transient state with a flip angle lower than 180° , followed by ramping down to a lower FA while acquiring the outer k-space lines. The 3D T_2 -TIDE images are acquired faster than 3D FSE by using a spiral-out phase encode ordering in the k_y - k_z plane of the 3D Cartesian k-space trajectory (82) to efficiently sample the central 3D k-space lines with T_2 contrast. Image sharpness is improved by implementing a multi-shot interleaved acquisition scheme. This k-space acquisition scheme also eliminates the need for partial Fourier acquisitions to control the T_2 weighting as done for 2D T_2 -TIDE or 3D FSE. Furthermore, the acquisition of outer k-space lines with a lower FA steady-state bSSFP approach permits extended echo train durations compared to FSE.

8.2 THEORY

The decay of the transient signal (M_{xy}) for on-resonance spins in bSSFP, with perfectly balanced gradients and a preparation pulse of $\alpha/2$ applied for a duration of $TR/2$ (15) can be expressed as

$$M_{xy}(n) = \left(\sin\left(\frac{\alpha}{2}\right) M_0 - M_{ss} \right) \lambda^n + M_{ss} \quad [8.1]$$

where n is the echo number, α is the flip angle, M_0 is the proton density, M_{ss} is the steady-state bSSFP signal, and the decay rate (λ) of the *transient signal* is given as

$$\lambda = E_2 \sin^2(\alpha/2) + E_1 \cos^2(\alpha/2) \quad [8.2]$$

with $E_{1,2} = \exp(-TR/T_{1,2})$. λ is purely T_2 weighted if $\alpha=180^\circ$, but a 180° flip angle is not practicable for extended echo trains due to SAR limitations. T_2 -weighting, however, can also be attained when $TR/T_1 \sim 0$ (i.e., $E_1 \sim 1$). This approximation holds at higher field strengths due to the

increased T_1 (83) and when using a short TR, which is preferred when using bSSFP to reduce off-resonance induced banding artifacts and improve sequence efficiency. Fig. 8.1a shows the simulation of the bSSFP transient signal for the 50th echo with TR=4.84ms, TE=2.42ms, and $\alpha=60^\circ$ for a broad range of T_1 s (100ms to 3000ms) and a broad range of T_2 s (30ms to 300ms). The 50th echo was chosen to demonstrate the achievable contrast for the chosen T_2 s. Fig. 8.1b shows the percent signal change between the simulations shown in Fig. 8.1a and the simulation for the pure T_2 decay signal, which was simulated with $T_1=5000$ ms to ensure $TR/T_1 \sim 0$ (i.e. $E_1 \sim 1$). Iso-contours (white curves) for 10% and 20% signal differences are highlighted. Note that as T_1 and T_2 decrease, the percent signal difference becomes larger. Hence for prostate tissues with $T_1 \sim 1500$ ms, the percent signal difference is 15% for $T_2=50$ ms and decreases with increasing T_2 .

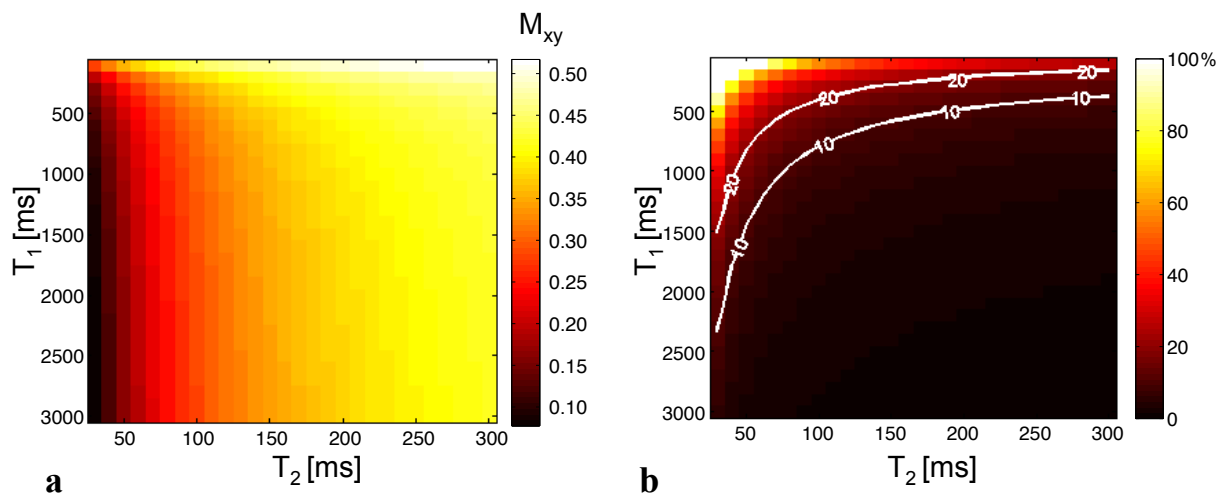


Figure 8.1: a) The simulated signal of the 50th echo and FA=60° for a range of T_1 s from 100ms to 3000ms in steps of 100ms and range of T_2 s from 30ms to 300ms in steps of 50ms. b) The percent signal difference between the signal in a) and pure T_2 decay simulated with $T_1=5000$ ms shows that for tissues with long T_1 s, the T_2 weighting is similar to pure T_2 decay. However, as T_1 s and T_2 s become shorter, the T_2 weighting of the signal decreases.

METHODS

8.3 3D T_2 -TIDE Image Acquisition Scheme

The flip angle scheme for 3D T_2 -TIDE is similar to the 2D T_2 -TIDE scheme. Both approaches use preparation pulses to control the T_2 weighting, followed by image acquisition (Fig. 8.2a). An $\alpha_{high}/2$ preparation pulse is followed by N_{prep} preparation pulses at α_{high} to control the T_2 weighting of the images; increasing N_{prep} increases the T_2 weighting. This is followed by data acquisition using α_{high} to maintain the T_2 weighting, then smoothly ramped down (17) to a lower flip angle α_{low} , which reduces SAR. The α_{high} is lower in 3D T_2 -TIDE compared to 2D T_2 -TIDE ($\alpha_{high}=180^\circ$) to reduce the SAR for 3D acquisitions in addition to maintaining the T_2 contrast (see 8.2 Theory).

The image acquisition duration of 3D T_2 -TIDE is made faster by acquiring the 3D Cartesian k-space in the k_y - k_z plane using a spiral-out phase encode ordering (82). The acquisition pattern is designed to acquire the 3D central k-space lines with α_{high} thereby maintaining the T_2 contrast and moves outward in a spiral pattern to the high spatial frequency k-space lines, which are acquired with the steady-state bSSFP signal and concomitant T_2/T_1 weighting. Multi-shot or interleaved spiral-out phase encode ordering within the k_y - k_z plane is performed to distribute the transition of the transient signal across a broader range of spatial frequencies thereby improving the sharpness of the image compared to single-shot approaches, albeit at the cost of increased scan time. The multi-shot images are acquired by including a time delay (t_D) after each shot, which allows for recovery of the longitudinal magnetization (M_z) before acquisition of the subsequent shot.

8.4 Bloch Simulations

In order to understand parameter selection, image contrast, and spatial resolution, Bloch equation simulations of the 3D T_2 -TIDE sequence were performed in MATLAB (The Mathworks, Natick, MA). Simulations of the transverse magnetization (M_{xy}) for bSSFP were performed for

normal prostate tissue with $T_1/T_2=1500/150\text{ms}$ (84,85), $TR/TE=4.84/2.42\text{ ms}$, $N_{k_y}=230$, $N_{k_z}=48$, $\alpha_{high}=60$, $\alpha_{low}=30$, $N_{prep}=50$, $N_{high}=20$, $N_{ramp}=200$, and $t_D=1635\text{ms}$ for number of shots (N_{shot})=1 and $N_{shot}=24$. These simulation parameters are identical to that of the subsequent 3D T_2 -TIDE in vivo imaging experiments (Table 8.1). The signal profile within the k_y - k_z plane was generated by combining the simulated single-shot or multi-shot signal with the generated k_y - k_z spiral-out phase encoding trajectory pattern.

The maximum contrast between normal prostate tissue with $T_1/T_2=1500/150\text{ ms}$ and prostate tumor tissue with $T_1/T_2=1500/100\text{ ms}$ (84,85) was determined by performing signal difference simulations with constant FA scheme ($\alpha_{high} = \alpha_{low}$) for a range of α_{high} varying from 10° to 180° and $N_{prep}=1$ to 150 with $TR/TE=4.84/2.42\text{ ms}$. These simulations were performed to determine the N_{prep} required for maximum signal contrast with the maximum achievable α_{high} determined by the SAR limitations.

The T_1 contributions to the 3D T_2 -TIDE signal were simulated for prostate tissue with $T_1/T_2=1500/150\text{ms}$, muscle tissue ($T_1/T_2=900/30\text{ ms}$) and fat tissue ($T_1/T_2=382/68\text{ ms}$ with off-resonance of 440Hz) (83) using the imaging parameters identical to the previous simulations. The signal evolution for each echo was compared to pure T_2 weighted simulations with identical T_2 s, but with long $T_1=5000\text{ms}$, which ensures $TR/T_1 \sim 0$ (i.e., $E_1 \sim 1$ in Eqn. 2).

The effect of N_{shot} on the point spread function (PSF) was determined by simulating the signal (M_{xy}) for normal prostate tissue using imaging parameters identical to the 3D T_2 -TIDE in vivo imaging experiments (Table 8.1) and $N_{shot}=1, 16, 24$, and 48 . The multi-shot PSF was also compared to the PSF of 3D steady-state bSSFP signal. The inverse Fourier transform of the signal resulted in the 2D PSF in k_y - k_z plane for each N_{shot} .

8.5 In Vivo Imaging

Our Institutional Review Board approved the protocol and written informed consent was obtained from all subjects prior the imaging. All images were acquired on a 3T scanner (Trio,

Siemens Medical Solutions, Erlangen, Germany) using a six-channel anterior coil and six-channel posterior spine matrix for prostate imaging. Prostate images were acquired in 10 healthy male subjects (N=10, age: 29±5 years) using 3D FSE, 2D multi-slice FSE, 3D T₂-TIDE, and 3D bSSFP to compare their signal differences. The imaging parameters for each of these acquisitions are summarized in Table 8.1. Separate noise scans (3,86) with identical imaging parameters without applied RF pulses were acquired for 3D FSE and 3D T₂-TIDE sequences to estimate the standard deviation of the noise for signal to noise ratio (SNR) calculations.

Images were also acquired with different N_{prep}=10, 25, 60 and 100 with constant N_{shot}=24 in a subset of five healthy subjects to demonstrate the different T₂ weighting achievable with 3D T₂-TIDE. The dependence of the PSF on N_{shot} was demonstrated by acquiring 3D T₂-TIDE images with different N_{shot}=1, 2, 4, 8, 16, 24 and 48 with constant N_{prep}=50. The other imaging parameters for these acquisitions were identical to the 3D T₂-TIDE acquisition parameters mentioned in Table 8.1 except the phase encoding direction was changed to anterior to posterior with 0-13% phase oversampling based on the subject and without GRAPPA, averages, and partial Fourier.

	2D FSE	3D FSE	3D T ₂ -TIDE	3D bSSFP
FOV (mm)	200×200	200×200	200×200	200×200
Resolution (mm)	0.6×0.6×3.0	0.9×0.8×1.5	0.9×0.8×1.5	0.9×0.8×1.5
Acquisition matrix	320×310	256×230	256×230	256×230
Phase oversampling (%)	100%	100%	100%	0%
Slice oversampling (%)	-	20%	20%	20%
Slice thickness (mm)	3.0	1.5	1.5	1.5
Interpolated Slices	20	60	60	60
Slices	20	48	48	48
BW (Hz/px)	200	315	930	930

Flip Angle	90°/150°	90°/110°	VFA	30-35°
PE direction	R to L	R to L	R to L	A to P
TR/TE (ms)	4000/101	2200/200	4.84/2.42	4.56/2.28
Echo spacing (ms)	11.2	6.14	4.84	4.56
Echo Train Duration (ms)	280	565	1112	-
GRAPPA factor/Ref lines	2/32	2/24	2/24	-
Partial Fourier	-	~6/8	6/8	-
Averages	2	2	2	1
T_{acq} (min)	3:38	7:02	2:54	0:56
SAR (W/kg)	1.5±0.2	1.5±0.2	1.6±0.2	1.8±0.3
Delay time, t _D (ms)	3720	1635	1635	-
N _{shots}	-	-	24	-

Table 8.1: Prostate imaging parameters for the different sequences. Phase encoding (PE) direction of A to P indicates Anterior to Posterior and R to L indicates Right to Left.

8.6 In Vivo Data Analysis

The SNR was calculated as the ratio of the mean signal to standard deviation of the noise from the noise scan (86) in five different regions: peri-prostatic fat, gluteal fat, left peripheral zone, right peripheral zone, and anterior fibromuscular stroma. The SNR was divided by

$\sqrt{\frac{2}{4-\pi}} = 1.53$ to account for the Rayleigh distribution of the noise (4). The regions of interest

(ROIs) were drawn in a single slice of the 3D FSE images for each of the 10 healthy subjects and copied to the identical slice in 3D T₂-TIDE and their corresponding noise scans. This was performed by a urologist having read over 1000 prostate MRI studies. The SNR efficiency

was calculated as the ratio of the SNR to the square root of the acquisition duration in minutes. The CNR was calculated between the anterior fibromuscular stroma and the peripheral zone as the difference between their SNR, the anterior fibromuscular stroma being consistently low signal and peripheral zone high signal in normal subjects. The SNR of the peripheral zone was calculated as the average of the SNRs of the left and right peripheral zone. The CNR efficiency was calculated as the ratio of the CNR to the square root of the acquisition duration in minutes. A statistical comparison between the SNR efficiency of the 3D FSE and 3D T₂-TIDE was calculated using a paired Student t-test for the five different regions with $P < 0.05$. The t-test values were Holm-Sidak post-hoc corrected.

8.7 RESULTS

Simulation Results

Simulated 3D T₂-TIDE images of the signal in the k_y - k_z plane were generated using a VFA scheme (Fig. 8.2a) with interleaved spiral-out phase encode ordering in the k_y - k_z plane. For simulated prostate tissue, the signal (M_{xy}) in the k_y - k_z plane for $N_{\text{shot}}=1$ and the corresponding VFA scheme (Fig. 8.2b-c) shows that the center of 3D k-space was acquired with the transient bSSFP signal and the outer k-space lines were acquired with the steady-state bSSFP signal. The corresponding signal and FA scheme for $N_{\text{shot}}=24$ are shown in Fig. 8.2d-e. Multi-shot 3D T₂-TIDE was used to increase the percent of the central k_y - k_z phase encodes acquired with the transient signal.

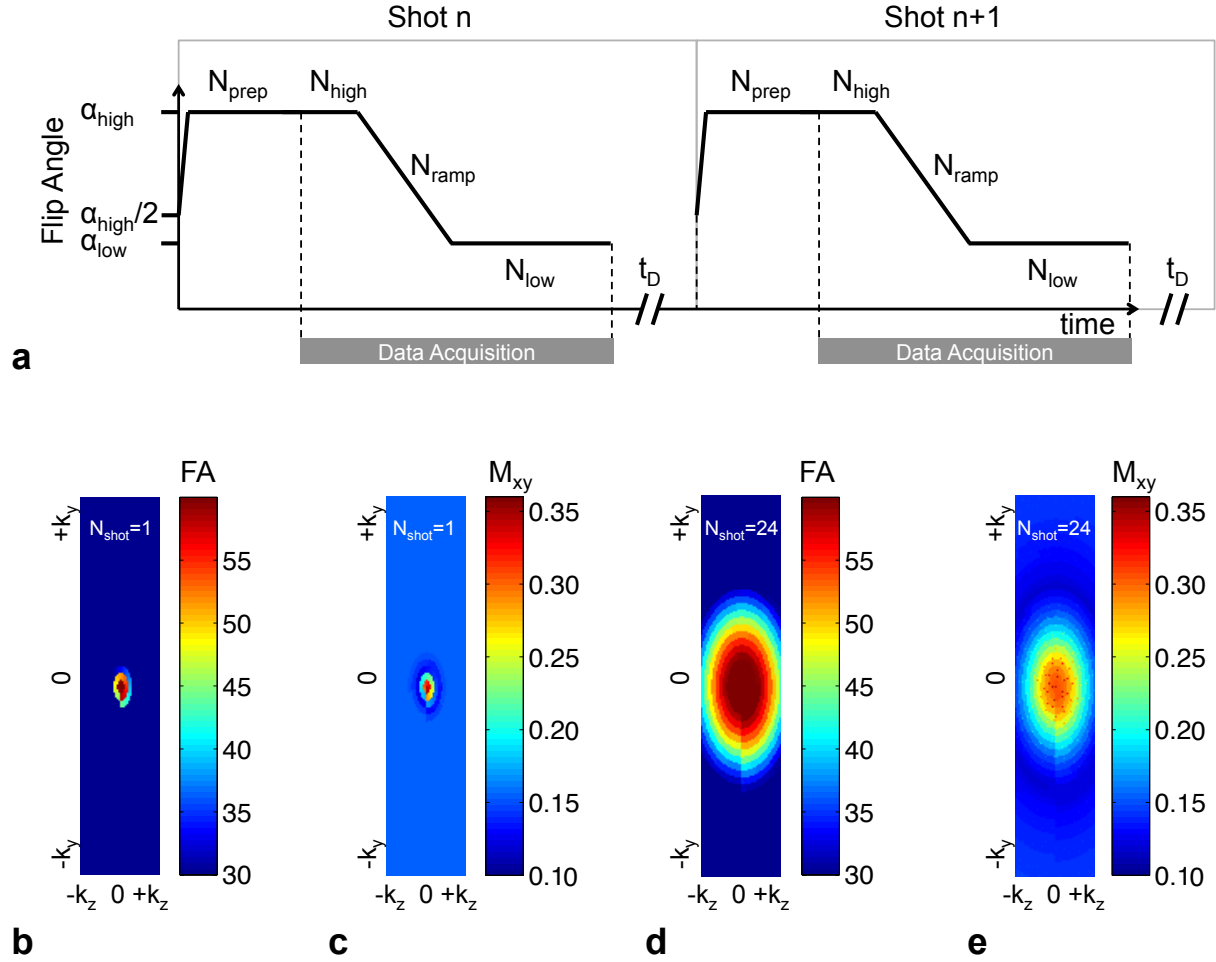


Figure 8.2: a) Block diagram showing the flip angle (FA) scheme of the interleaved 3D T_2 -TIDE sequence. The $\alpha_{high}/2$ prep pulse is followed by N_{prep} α_{high} preparation pulses to control the T_2 weighting of the image. The images are acquired with N_{high} α_{high} pulses to maintain the T_2 contrast of the image and are smoothly ramped down to α_{low} to reduce the SAR. A delay of t_D is applied for the recovery of M_z and is followed by the acquisition of the next shot. Simulation of tissue with $T_1/T_2=1500/150\text{ms}$ and b) $N_{shot}=1$ showing the FA variation along spiral sampling in $ky-k_z$ plane which (c) generates a signal and the corresponding (d) FA and (e) signal for $N_{shot}=24$.

The T_2 contrast of the 3D T_2 -TIDE images was governed by the choice of α_{high} and N_{prep} that were used to specify the VFA scheme. Fig. 8.3 shows the transient bSSFP signal simulation of

the contrast between the normal prostate tissue and tumor tissue for a range of α_{high} and N_{prep} . The simulation with $\alpha_{high}=180^\circ$ corresponds to the T_2 contrast achievable in a spin echo sequence by varying the effective TE (i.e N_{prep}). The α_{high} used for the 3D T_2 -TIDE acquisitions was determined by the SAR limitation at 3T. Hence, for a given α_{high} , N_{prep} can be chosen by following the contrast curve from $\alpha_{high}=180^\circ$ to the achievable α_{high} . For example, by choosing $\alpha_{high}=74^\circ$ and $N_{prep}=51$, contrast of 0.08 is produced which is also achievable using $\alpha_{high}=180^\circ$ and $N_{prep}=7$ (shown as red dots in Fig. 8.3). The black dot indicates the maximum contrast achieved using $\alpha_{high}=180^\circ$, which cannot be obtained by using a $\alpha_{high}<180^\circ$, but a very similar contrast can be attained with α_{high} as low as 140° .

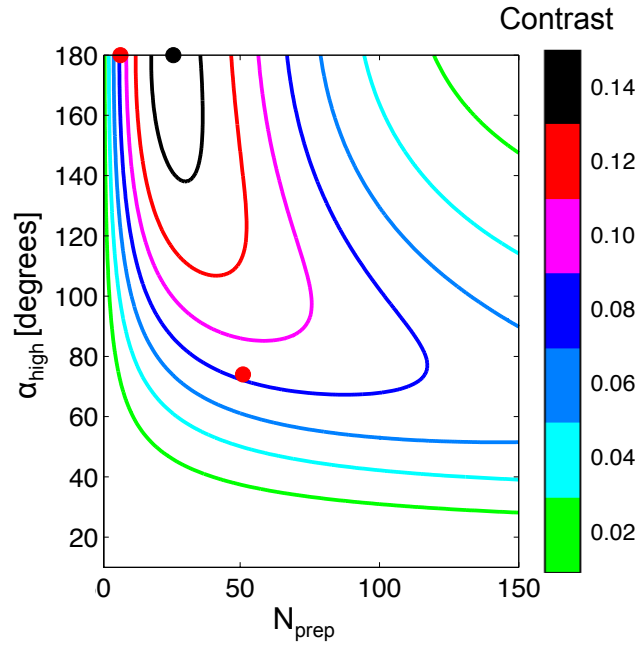


Figure 8.3: Simulation of contrast (signal difference) between tissues with $T_1/T_2=1500/150\text{ms}$ and $T_1/T_2=1500/100\text{ms}$ for a range of α_{high} from 10° to 180° and range of N_{prep} from 1 to 150 pulses. The maximum contrast of 0.15 (black dot) achieved by spin echo sequence using α_{high} of 180° and $N_{prep}=26$, however cannot be achieved by using a α_{high} lower than 180° . The contrast of 0.08 (red dot) corresponding to spin echo

sequence with $\alpha_{\text{high}}=180^\circ$ and $N_{\text{prep}}=7$ can be achieved with a lower $\alpha_{\text{high}}=74^\circ$ with $N_{\text{prep}}=51$ pulses.

Fig. 8.4 shows the signal evolution of the transient signal for prostate tissue, muscle, and fat (with off-resonance) and compares their respective signal evolutions to tissues with identical T_2 s, but with long $T_1=5000\text{ms}$ in order to simulate pure T_2 decay. When $N_{\text{echoes}}=N_{\text{prep}}$, the transient signal for prostate tissue ($T_1=1500\text{ms}$) and muscle ($T_1=900\text{ms}$) are similar to the pure T_2 decay due to their long T_1 . The fat signal ($T_1=382\text{ms}$), however, is higher in 3D T_2 -TIDE compared to pure T_2 decay as a consequence of both the short T_1 and off-resonance.

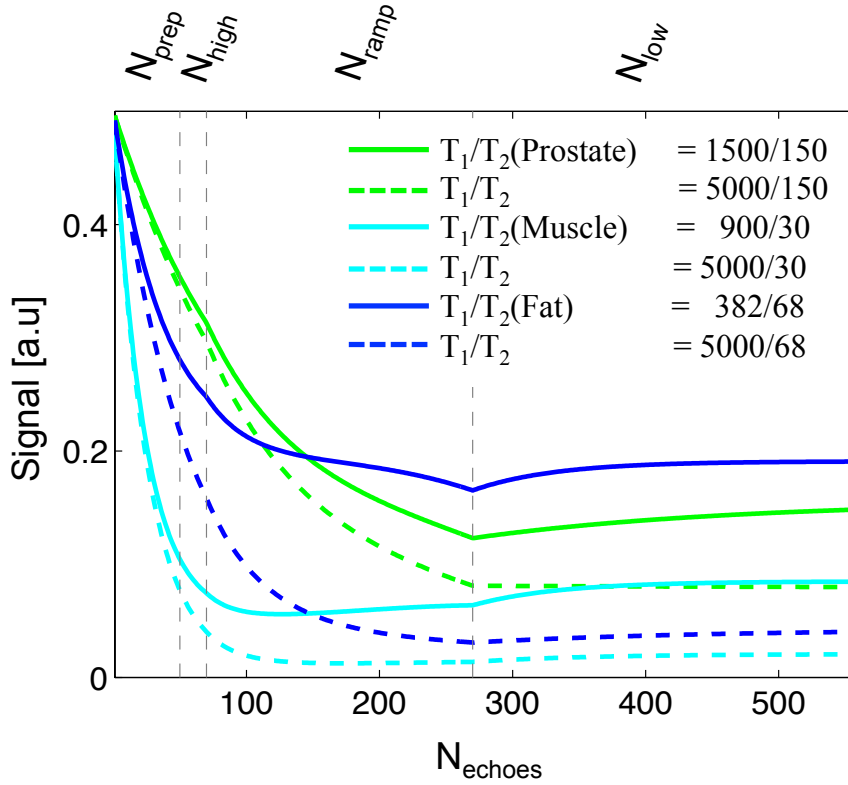


Figure 8.4: Signal evolution of prostate tissue (green), muscle (cyan), and fat (blue) for a single shot with $\alpha_{\text{high}}=60^\circ$, $\alpha_{\text{low}}=30^\circ$, $N_{\text{prep}}=50$, $N_{\text{high}}=20$ and $N_{\text{ramp}}=200$. The fat signal was simulated with a off-resonant frequency of 440Hz but the other tissues were simulated at

on-resonance. The colored dashed lines represent samples with T_2 s identical to the solid colored lines but with long $T_1=5000$ ms.

The PSF of the 3D T_2 -TIDE images was improved by increasing N_{shot} . Fig. 8.5a-b shows the simulation of the 2D PSF for $N_{\text{shot}}=1$ and $N_{\text{shot}}=48$. The line profiles along the center of the y- and z-directions for 3D steady-state bSSFP signal, $N_{\text{shot}}=1, 16, 24$ and 48 are shown in Fig. 8.5c-d. The side lobes of the PSF decreases with increasing N_{shot} , which shows that increasing N_{shot} improves the PSF along the y direction, albeit at the cost of extended scan times. Similar to the y-direction, the side lobes of the multi-shot acquisitions are attenuated in the z-direction compared to $N_{\text{shot}}=1$. However, the main lobes of the multi-shot acquisitions are similar to each other.

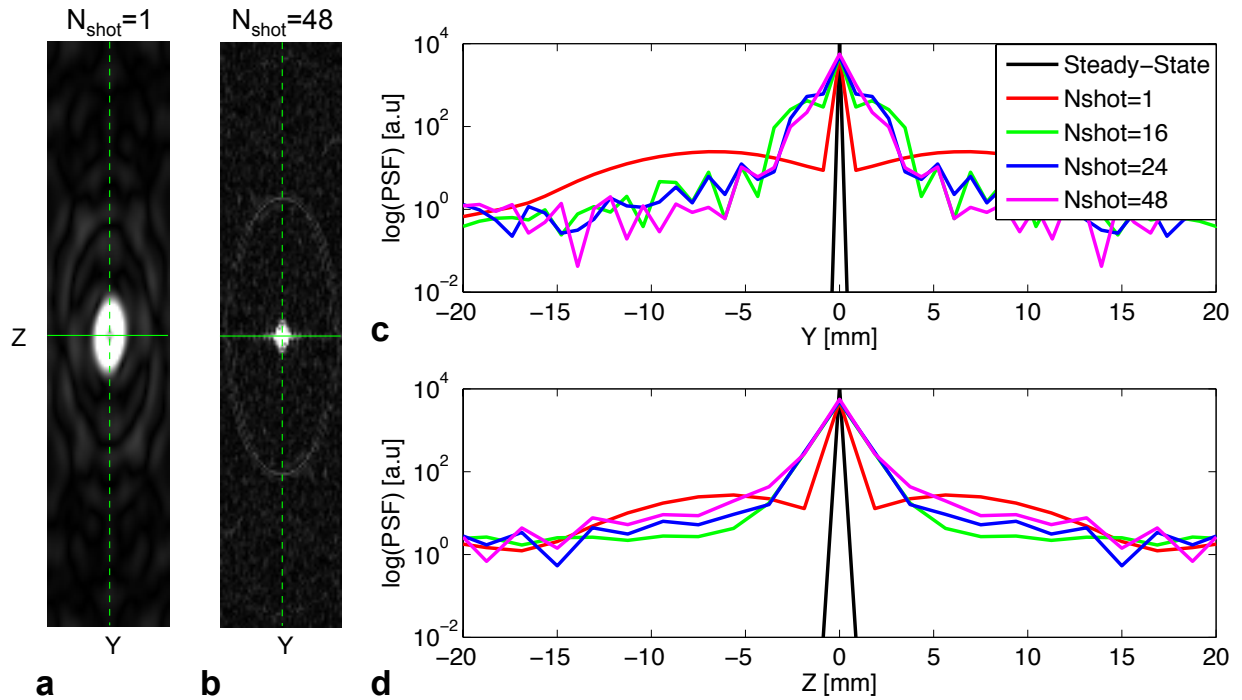


Figure 8.5: a-b) Image of the 2D PSF for a tissue with $T_1/T_2=1500/150\text{ms}$, $N_{k_y}=230$, $N_{k_z}=48$, $\alpha_{\text{high}}=60^\circ$, $\alpha_{\text{low}}=30^\circ$, $N_{\text{prep}}=50$, $N_{\text{high}}=20$, $N_{\text{ramp}}=200$ and $N_{\text{shot}}=1, 48$. Line profile of the PSF in logarithmic scale along the center in (c) y- and (d) z-direction with steady-

state signal (black), $N_{\text{shot}}=1$ (red), $N_{\text{shot}}=16$ (green), $N_{\text{shot}}=24$ (blue) and $N_{\text{shot}}=48$ (magenta). Interleaved (multi-shot) acquisition has reduced side lobes and hence improved sharpness compared to $N_{\text{shot}}=1$.

In Vivo Results

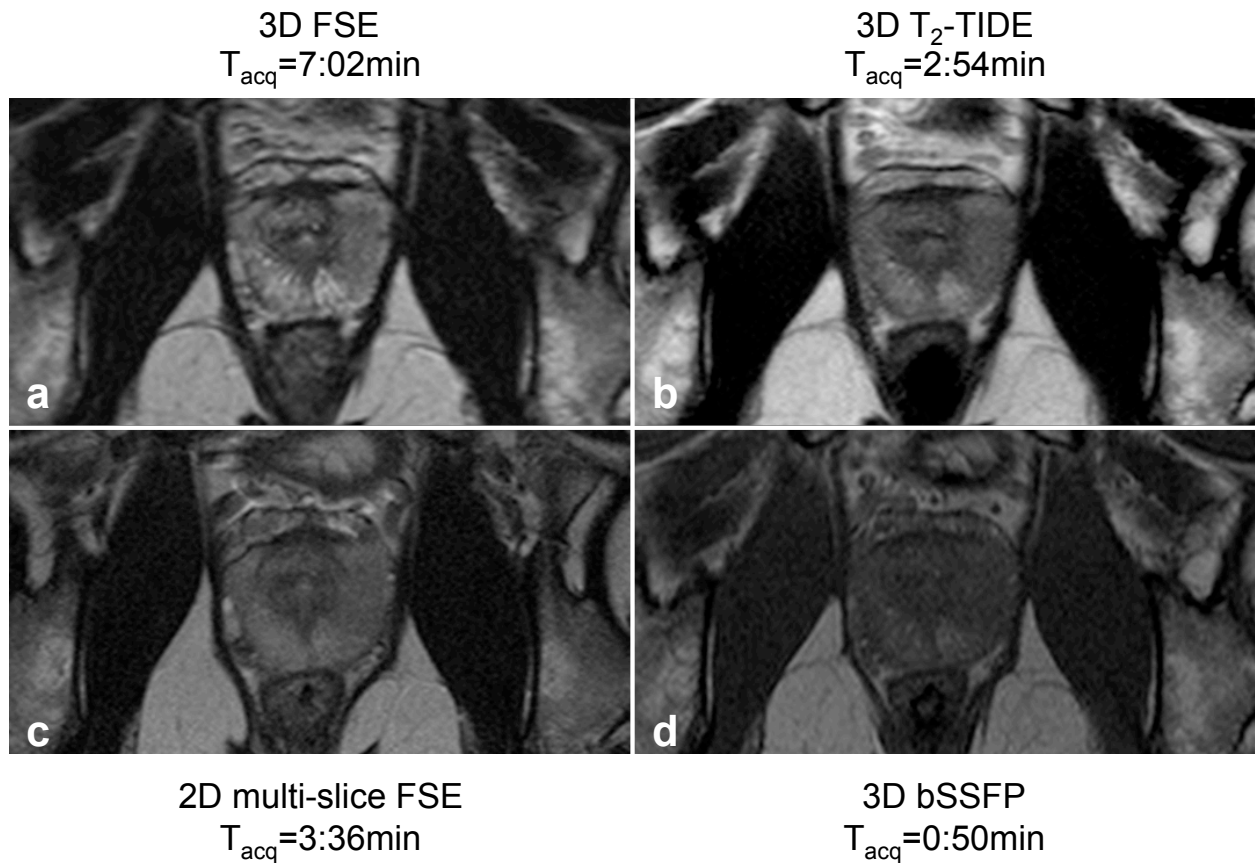


Figure 8.6: Single slice images of a healthy subject using a) clinical 3D FSE b) 3D T_2 -TIDE c) 2D multi-slice FSE and d) 3D bSSFP. The 3D T_2 -TIDE images are T_2 weighted similar to 3D FSE and 2D multi-slice FSE with clear delineation of the prostate “capsule”.

Fig. 8.6 compares axial prostate images acquired in a healthy subject using 3D FSE, 3D T_2 -TIDE, 2D multi-slice FSE and 3D bSSFP. The 3D T_2 -TIDE images are T_2 weighted similar to 3D

FSE and 2D multi-slice FSE with clear delineation of the prostate “capsule”. The acquisition duration of 3D T_2 -TIDE was 2:54 minutes compared to 3D FSE acquisition duration of 7:02 minutes. Compared to the T_2 weighted images, the 3D bSSFP images show that the contrast between the anterior fibro muscular stroma and the peripheral zone and tissue signal heterogeneity within the prostate are qualitatively reduced.

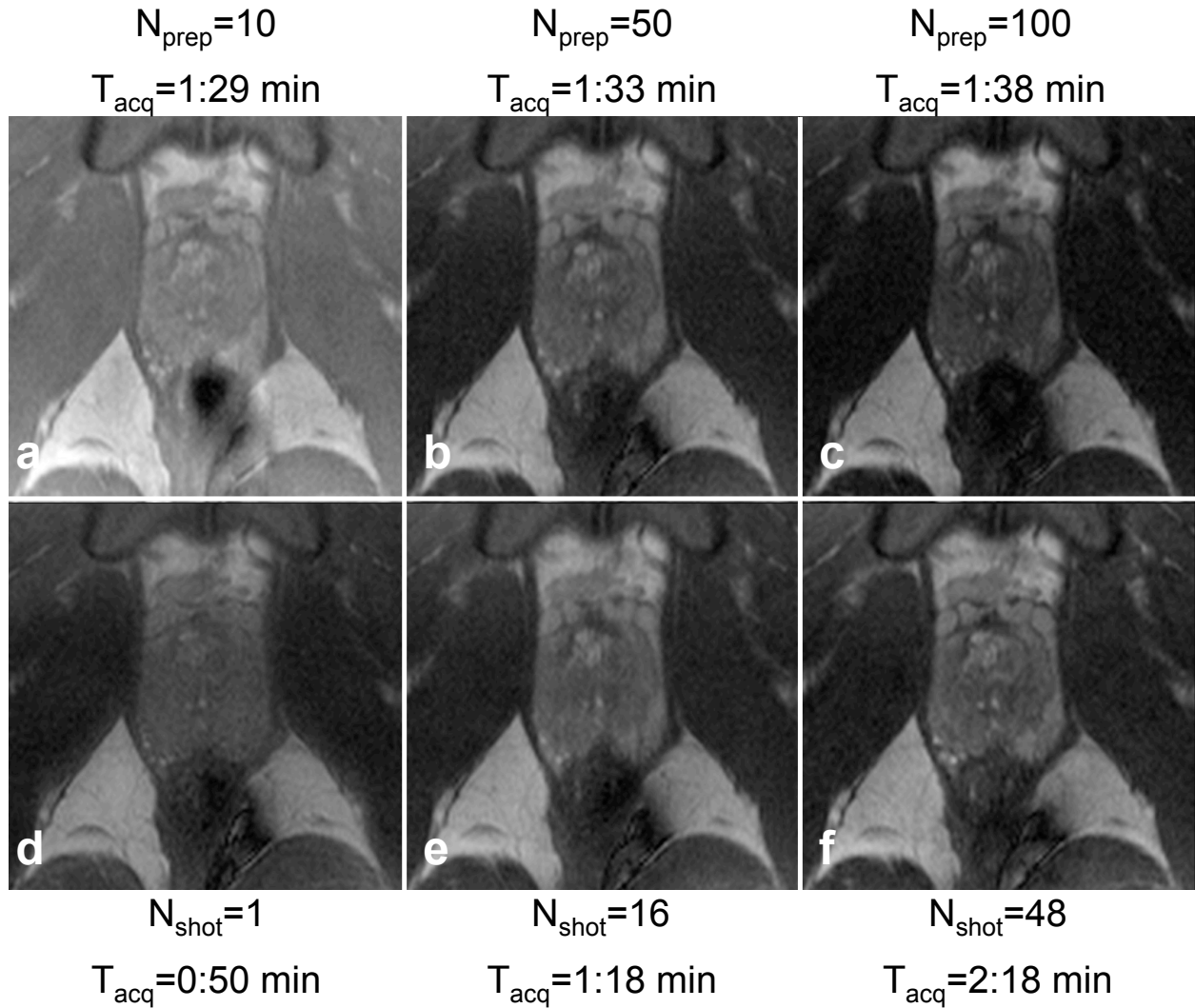


Figure 8.7: Single slice from 3D T_2 -TIDE images from a healthy subject showing the differences in T_2 weighting due to a) $N_{\text{prep}}=10$, b) $N_{\text{prep}}=50$ and c) $N_{\text{prep}}=100$. Higher N_{prep} results in increased T_2 weighting. The images in the bottom row shows the change in the sharpness of the image due to d) $N_{\text{shot}}=1$, e) $N_{\text{shot}}=16$ and d) $N_{\text{shot}}=48$. Higher N_{shot} results

in sharper images due to the improvement in PSF. All the images have the same window level.

Fig. 8.7 a-c shows 3D T₂-TIDE images acquired with different T₂ weighting by changing N_{prep}=10, 50 and 100. Lower N_{prep} results in reduced T₂ contrast with similar image sharpness, whereas increasing N_{prep} improves T₂ contrast. All images have the same window level. Fig. 8.7 d-f shows 3D T₂-TIDE images acquired with varying N_{shot}=1, 16 and 48. The delineation of the prostate “capsule” is improved with increasing N_{shot} due to improvement in the PSF, but with a penalty of increased acquisition duration as shown in each figure.

Fig. 8.8 compares the acquisition of 3D T₂-TIDE to 3D FSE for images acquired in the axial plane and reformatted into the coronal and sagittal planes. Overall, the image quality and contrast is very similar, but the 3D T₂-TIDE images are acquired significantly faster. In particular, note that the prostate “capsule” is clearly depicted in both of these acquisitions in all the imaging planes. The isovolumetric resolution allows for improved fidelity in multimodal image fusion and multiplanar reformations may obviate the need for acquisition of additional pulse sequences to visualize those planes.

The SNR efficiency of 3D T₂-TIDE was compared to 3D FSE in five different regions from images acquired in the healthy subjects (N=10). The SNR efficiency in all measured tissues: peri-prostatic fat= 45±12 vs. 31±7 (*P*<0.01), gluteal fat= 48±8 vs. 41±10 (*P*=0.12), right peripheral zone= 20±4 vs. 16±8 (*P*=0.12), left peripheral zone= 17±2 vs. 12±3 (*P*<0.01), and anterior fibro muscular stroma= 12±4 vs. 4±2 (*P*<0.01). The SNR efficiency of the anterior fibro muscular stroma, peri-prostatic fat and left-peripheral zone was significantly higher in 3D T₂-TIDE compared to 3D FSE. The CNR efficiency between the anterior fibro muscular stroma and peripheral zone using 3D T₂-TIDE was 10±6 and for 3D FSE it was 16±8 (*P*=0.03).

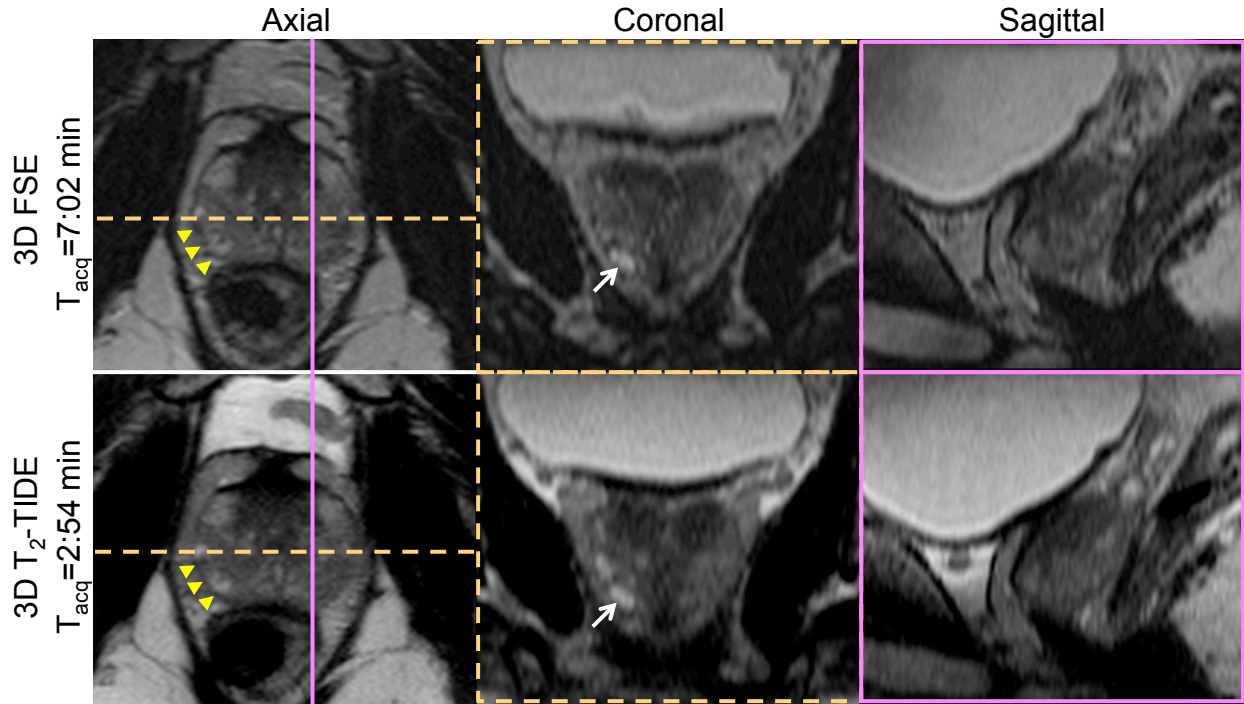


Figure 8.8: 3D FSE (top row) and 3D T_2 -TIDE (bottom row) acquired in axial plane in a healthy subject showing clear delineation of the prostate capsule (yellow arrows). The reformatted images in coronal and sagittal plane also show good definition of features such as cystic benign nodule (white arrow) within the prostate.

8.8 DISCUSSION

3D T_2 -TIDE was developed and evaluated for fast 3D T_2 -weighted prostate imaging at 3T. We demonstrated that images with an acquisition duration of 2:54 minutes compared very favorably to 3D FSE with an acquisition duration of 7:02 minutes and matched imaging parameters. The 3D T_2 -TIDE images were acquired during the transient state of the bSSFP signal to control the T_2 weighting with multi-shot spiral-out phase encode ordering in the k_y - k_z plane of the 3D Cartesian trajectory, which enabled acquisition of the central k-space during the transient signal and the outer k-space during the steady state of bSSFP. This approach balanced maintaining T_2 weighting, preserving image resolution, and scanning fast.

In principle, pure T_2 weighting (identical to a spin echo) is possible with bSSFP imaging during the transient state with $FA=180^\circ$. 3D imaging with $FA=180^\circ$ for extended echo trains with short TRs, however, is not possible at high field strengths ($\geq 3T$) due to the SAR limitation. 3D T_2 weighting is still possible with $FA < 180^\circ$ if the tissue T_1 is long compared to TR. Bloch simulation with $FA=60^\circ$ (Fig. 8.1a-b) showed that the images will be T_2 weighted for long T_1 s with minimal percent signal difference compared to pure T_2 weighted signal. As both the T_1 and T_2 shorten, the T_2 contrast between tissues decreases.

The 3D T_2 -TIDE signal profile in the first shot is higher than the signal profile in the subsequent shots which is visible, in the signal simulation of $N_{shot}=24$, as speckles in Fig. 8.2e. This occurs because of the duration required for the 3D T_2 -TIDE signal to reach a dynamic steady state between the shots (45,54). The effect of the high signal in the first shot compared to the subsequent shots was analyzed by acquiring 3D T_2 -TIDE prostate images in healthy subjects using a discarded preparation shot. These images were compared to identical 3D T_2 -TIDE acquisitions without discarding the first shot and the no qualitative effects on the image quality were observed. Hence, all the 3D T_2 -TIDE in vivo images was acquired without the discarded shot in order to scan faster.

The maximum T_2 contrast achieved with $\alpha_{high}=180^\circ$ will be higher than the maximum contrast that is achieved using a lower FA ($\alpha_{high}=60^\circ$) (Fig. 8.3). Hence, the CNR and the CNR efficiency between the anterior fibro muscular stroma and the peripheral zone was reduced using 3D T_2 -TIDE ($\alpha_{high}=60^\circ$) compared to 3D FSE ($\alpha=110^\circ$). However, there was no loss of the difference between high signal in the peripheral zone and low signal in the anterior fibromuscular stroma and “capsule” qualitatively.

The 3D T_2 -TIDE images were acquired during the transient state of the bSSFP signal to maintain the T_2 contrast. However, as the signal is not constant during the k-space filling, the PSF of 3D T_2 -TIDE is broader compared to the 3D bSSFP imaging (Fig. 8.5c-d). The PSF is

also dependent on the N_{shot} and the spiral-out phase encode trajectory pattern in the Cartesian k_y - k_z plane. Due to the lower resolution along the z -direction compared to the y -direction, the choice of N_{shot} impacts the PSF along y and z differently (Fig. 8.5c-d). Different algorithms can be used for sampling the spiral-out pattern on the k_y - k_z Cartesian grid, which may improve the PSF in the y - and z -direction uniformly. Worters et al., (53) have used Bloch simulations for designing a VFA scheme that produces constant bSSFP transverse magnetization. Similar simulations may be used to design VFA schemes that reduce the slope of transient bSSFP signal for 3D T_2 -TIDE imaging, thereby improving the PSF.

The T_2 contrast in FSE sequences is mainly controlled by the partial Fourier factor. The effective TE can be further reduced by the use of parallel imaging. In 3D T_2 -TIDE, however, the T_2 contrast is controlled by N_{prep} and does not depend on the parallel imaging and partial Fourier factors. Herein, the in vivo 3D T_2 -TIDE experiments used both partial Fourier and parallel imaging factors identical to 3D FSE for fair comparison of acquisition duration and SNR between these sequences. The spiral-out phase encode ordering in the k_y - k_z Cartesian plane of 3D T_2 -TIDE enables the use of $N_{\text{shot}} \leq N_{kz}$, unlike other conventional 3D linear techniques using $N_{\text{shot}} \geq N_{kz}$. For example, if the N_{shot} is decreased, the images can be acquired even faster but at the cost of broader PSF or increased image blurriness. This may be useful for monitoring 3D T_2 changes during interventional procedures.

Prostate images are clinically acquired in the axial plane with phase encoding along the right to left (RL) direction to reduce rectal motion artifacts, which occur predominantly in the anterior to posterior direction. As the FOV in RL direction is $\sim 2\times$ larger than the FOV in AP direction, the acquisition duration for the 3D prostate imaging is nearly doubled compared to swapping the phase and frequency axes. If the phase encoding duration is chosen to be along the AP direction, then the acquisition duration of 3D T_2 -TIDE can be further reduced to 1:33 min (Fig. 8.7b), which may reduce the prevalence of the apparent rectal motion artifacts and may limit the need for glucagon.

In this paper, 3D T_2 -TIDE has been applied for fast 3D T_2 weighted imaging of the prostate. Further evaluation is needed for different applications of 3D T_2 weighted imaging including the abdomen, breast, uterine tumors (87,88), spine (89), ganglion cysts (90), and ankle.

Limitations

The T_2 contrast in the 3D T_2 -TIDE images is due to acquisition of central k-space lines during the transient bSSFP signal that is T_2 weighted for a range of T_1 s and T_2 s based on the assumption that the image contrast is mainly contributed by the central k-space. This is especially true for large objects approaching the size of the FOV. However, as the object size decreases in the image domain, the region of the central k-space contributing to the image contrast increases. Hence, especially for small prostate tumors, the image contrast is due to both the transient signal and the steady-state signal. This property of 3D T_2 -TIDE is similar to other VFA acquisition techniques that use higher FA to acquire the central k-space relative to the outer k-space lines. Furthermore, as regards to image contrast the T_2 weighting in 3D T_2 -TIDE is preserved only for a range of T_1 s and T_2 s. Hence, 3D T_2 -TIDE may not produce sufficient T_2 weighting after contrast administration due to the shortening of the T_1 .

The 3D T_2 -TIDE images are susceptible to off-resonance induced banding artifacts and therefore require the use of shim gradients to reduce B_0 inhomogeneities and a short TR. The prostate images acquired in healthy subjects did not have banding artifacts when using the standard (i.e. *not* patient specific) shim. Susceptibility artifacts were also subtly pronounced in regions surrounding the rectum in the 3D T_2 -TIDE images compared to the 3D FSE.

The interleaved multi-shot 3D T_2 -TIDE acquisition with spiral-out phase encode ordering in k_y - k_z , improves the PSF by increasing the distribution of the transient signal in the middle of k_y - k_z . However, due to the delay between subsequent shots, any motion that occurs between shots may result in motion artifacts because the central k-space lines are partly acquired with each

shot. Further improvements, like oversampling of the central k_y - k_z space may reduce artifacts due to inter-shot motion.

8.9 CONCLUSION

3D T_2 -TIDE can be used for fast 3D T_2 weighted prostate imaging at 3T with acceptable image quality and ~58% reduction in acquisition duration compared to 3D FSE. The flexibility afforded by an interleaved shot strategy in 3D T_2 -TIDE enables trade-offs between acquisition speed and image sharpness.

CHAPTER 9

LOW SAR NON-CONTRAST MR ARTERIOGRAPHY OF THE LOWER LEG

The variable flip angle scheme for uniform signal excitation of bSSFP imaging (53) with RF phase alternation ($VUSE_{alt}$) is used to improve the spatial resolution of the image acquired during the transient state of bSSFP as described in Chapter 5.5. Here, we have used a similar principle to derive the VFA scheme for uniform signal excitation of a pulse sequence with balanced gradients along the three axes with no RF phase alteration bSSFP_{noalt} (2). Unlike the $VUSE_{alt}$, where the flip angle approaches 180° with increased echo number to maintain constant signal, the VFA scheme for bSSFP_{noalt} ($VUSE_{noalt}$) is not SAR intensive. The spectral profile of $VUSE_{noalt}$ has a distinct sharp on-resonance, with a sharp on-resonance band and a wide off-resonance band. This unique property of $VUSE_{noalt}$ is used for non-contrast enhanced MR arteriography of the lower leg. This work, titled “Very low SAR imaging of the lower leg using variable angle for uniform signal excitation (VUSE) and balanced SSFP without RF phase cycling” was, in part, presented at ISMRM, Melbourne, 2012, abstract: 2500.

9.1 INTRODUCTION

The bSSFP sequences have zero gradient dephasing between subsequent TRs due to the balanced gradients along all the three axes. The balanced SSFP signal can be created using RF excitation pulses with the same phase (without sign alteration) or with sign altered phase (2). The steady-state signal with the sign altered phase (bSSFP_{alt}) is higher than the signal without the sign altered phase (bSSFP_{noalt}) as shown in Eqns. 9.2-9.3 and hence is widely used clinically for its high signal-to-noise ratio (SNR) efficiency.

Variable flip angle (VFA) imaging has been used to reduce the specific absorption rate (SAR) of spin echo sequences (50,52) as well as to improve the spatial resolution (91), signal (54), contrast (55) of gradient echo imaging. Recently, a variable flip angle design for uniform signal

excitation (VUSE) with balanced SSFP and RF phase alternation (53) was designed to improve the spatial resolution of transient bSSFP images with a reduced preparation duration. The VFA scheme used to achieve constant transverse magnetization (M_{xy}) was calculated during transient imaging using matrix inversion of the Bloch equation (53), and is termed as $VUSE_{alt}$.

In this work, we iteratively calculate the flip angle required to provide constant M_{xy} for bSSFP without RF phase alternation termed as $VUSE_{noalt}$. The **objective** of this work is to design the $VUSE_{noalt}$ with SNR matched to $VUSE_{alt}$. The VFA train, calculated by matrix inversion of the Bloch equation, results in a very low flip angle train (and concomitantly very low SAR) with SNR similar to $VUSE_{alt}$ but high sensitivity to off-resonance.

We evaluated the $VUSE_{noalt}$ sequence for non-contrast arteriography of the lower leg owing to its inherent lower fat signal, and lower venous signal compared to arterial signal, due to off-resonance sensitivity of $VUSE_{noalt}$. We have also compared the contrast of $VUSE_{noalt}$ image with constant flip angle bSSFP and $VUSE_{alt}$.

9.2 THEORY

The variable flip angle profile for $VUSE_{noalt}$ can be calculated iteratively, similar to VUSE (53) using the following expression,

$$\tan \alpha = \frac{2 G_2 G_3 \pm \sqrt{(2 G_2 G_3)^2 - 4(H^2 - G_3^2)(H^2 - G_2^2)}}{2(H^2 - G_3^2)} \quad [9.1]$$

where $G_2 = E_2 M_{xy}$; $H = \frac{M_T}{E_2}$; $G_3 = E_1 \cdot M_z + (1 - E_1)M_0$; $E_{1,2} = e^{-\frac{TE}{T_{1,2}}}$

M_T is the desired transverse magnetization, M_{xy} and M_z are the current transverse and longitudinal magnetization respectively. Note that the Eqn. 9.1 is identical to Eqn. 5.1 of $VUSE_{alt}$. However, both G_2 and H are negative in $VUSE_{alt}$ due to RF sign alteration compared to $VUSE_{noalt}$. The derivation of Eqn. 9.1 is detailed in Appendix 9.8.

METHODS

The bSSFP pulse sequence without RF phase alternation is shown in Fig. 9.1a where the gradients along the three axes are balanced with zero RF phase cycling. The steady-state bSSFP signal with RF phase alternation ($bSSFP_{alt}$) and $bSSFP_{noalt}$ are given by the following:

$$bSSFP_{alt} = M_0 \sin \alpha \frac{1 - E_1}{1 - (E_1 - E_2) \cos \alpha - E_1 E_2} e^{-TE/T_2} \quad [9.2]$$

$$bSSFP_{noalt} = M_0 \sin \alpha \frac{1 - E_1}{1 - (E_1 + E_2) \cos \alpha + E_1 E_2} e^{-TE/T_2} \quad [9.3]$$

Note that the steady state signal of $bSSFP_{noalt}$ is lower than the steady-state signal of $bSSFP_{alt}$ due to the additional term in the denominator of Eqn. 9.3. The steady-state spectral profile of $bSSFP_{alt}$ and $bSSFP_{noalt}$ is shown in Fig. 9.1b for a tissue with $T_1/T_2=1000/1000$ ms, $TR=5.24$ ms and $TE=TR/2$. The spectral profile of the $bSSFP_{alt}$ has a maximum signal at on-resonance and minimal signal at off-resonance, compared to minimum on-resonance signal and maximum off-resonance signal for $bSSFP_{noalt}$. Note that the RF phase alternation shifts the spectral profile by 180° and increases the on-resonance steady-state signal.

The blood oxygenation level differences between the arterial blood and the venous blood results in changes in the susceptibility between the intra- and extra-vascular space. The frequency change due to blood oxygenation for a vessel parallel to the static field is given by (92)

$$\Delta f \approx 20 \text{ Hz} (1 - Y) \quad [9.4]$$

where Y is the oxygenation level in the vessel at 1.5T. For example, blood oxygenation of 75% results in off-resonance of 5 Hz. Hence there will be differences in the off-resonance or frequency shift between the arterial blood and the venous blood, which can be differentiated using $VUSE_{noalt}$ due to its high off-resonance sensitivity.

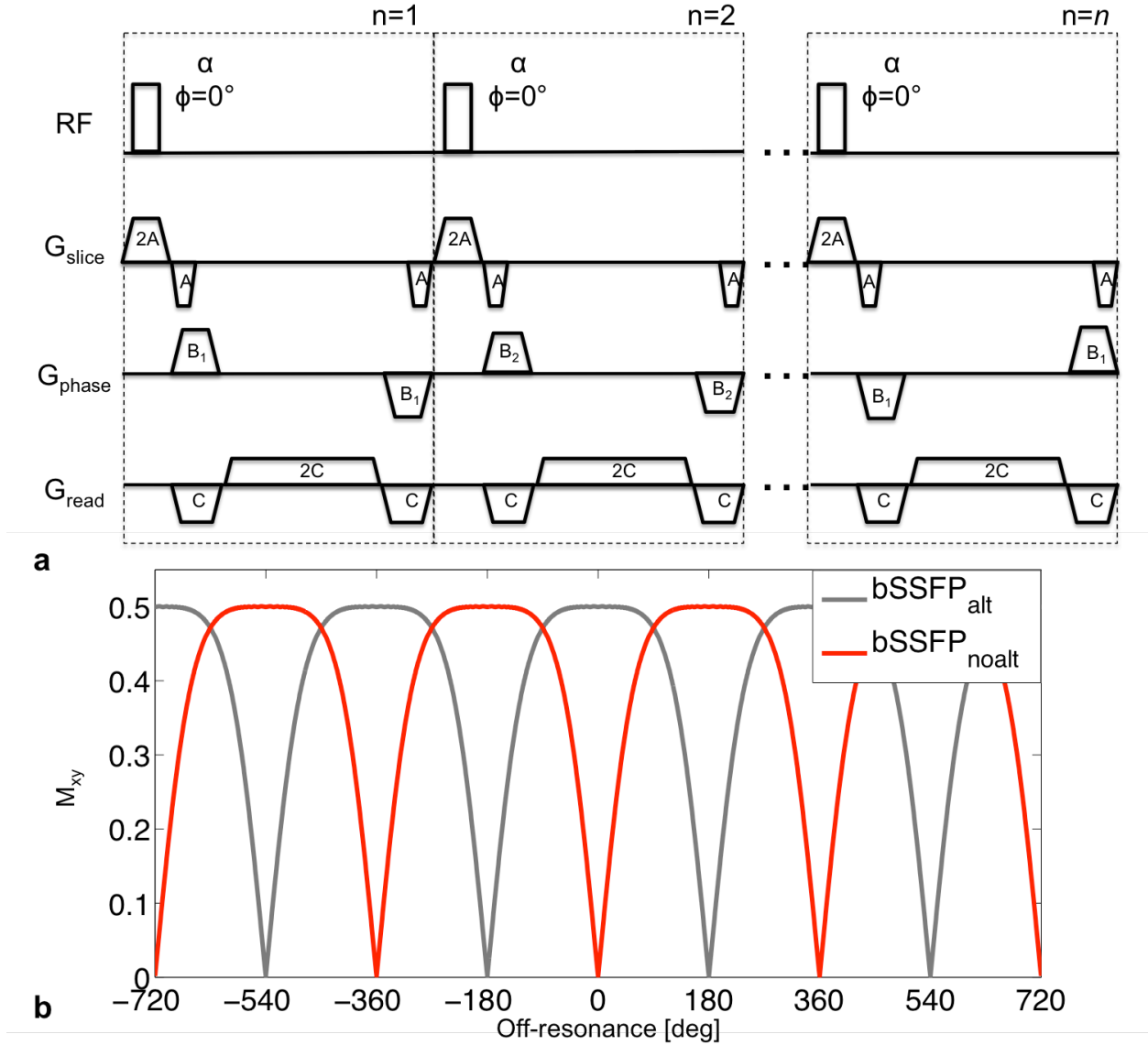


Figure 9.1: a) Sequence diagram of bSSFP_{noalt} with balanced gradients and no RF pulse phase alternation. (b) Simulation of the steady-state spectral profile of bSSFP_{alt} and bSSFP_{noalt}. The steady-state signal of bSSFP_{noalt} is lower during on-resonance and RF phase alternation shifts the spectral profile by 180°.

9.3 Bloch Equation Simulations

Bloch equation simulations were performed in MATLAB (The Mathworks, Natick, MA, USA). The VFA train with desired constant M_T as a function of the echo number was calculated for

arterial blood tissue with $T_1/T_2=1000/200$ ms, $TR=5.24$ ms, $TE=TR/2$, $M_0=1$, $M_T=0.7$ and initial flip angle of $\alpha_1 = \sin^{-1}M_T$. The resultant flip angle train calculated using Eqn. 9.1 was used to simulate the transverse and longitudinal magnetization of venous blood tissue with $T_1/T_2=1000/100$ ms and off-resonance of 5 Hz and 10 Hz and for fat tissue with $T_1/T_2= 288/165$ ms (93) and off-resonance of 220 Hz. The VFA train for $VUSE_{alt}$ was also calculated using Eqn. 5.1 for arterial blood tissue and the resultant flip angle scheme was used to simulate the transverse and longitudinal magnetization of each of the other tissues. Five Kaiser-Bessel prepatation pulses were used to stabilize the signal of $VUSE_{alt}$.

9.4 In Vivo Imaging

All the images were acquired on a 1.5T scanner (Avanto; Siemens Medical Solutions, Erlangen, Germany) with informed consent. Our Institutional Review Board approved the protocol. 2D multi-slice linearly interleaved, segmented images of the lower leg were acquired in three subjects (two male) using single shot bSSFP, segmented interleaved $VUSE_{alt}$, and $VUSE_{noalt}$ for appropriate comparison of SNR and SAR.

The imaging parameters were $FOV=150 \times 150$ mm, acquisition matrix= 512×512 , slice thickness = 5 mm, views per segment=20, $N_{slices}=15$, $TR=5.24$ ms, $BW=558$ Hz/px; and constant flip angle of 70° for bSSFP and variable flip angle train for $VUSE_{alt}$ and $VUSE_{noalt}$ calculated based on TR and segments for a desired $M_T=0.7$. The total acquisition duration for bSSFP, $VUSE_{alt}$ and $VUSE_{noalt}$ were 21s, 50s, and 50s respectively.

Data Analysis

Regions-of-interest were drawn over the artery, vein, muscle, fat and background regions on each of the subjects. The SNR was calculated as the ratio of the signal mean to the standard

deviation of background noise. The SNR was divided by a correction factor (4) of $\sqrt{\frac{2}{4-\pi}} = 1.53$, to account for the Rayleigh distribution of the noise.

9.5 RESULTS

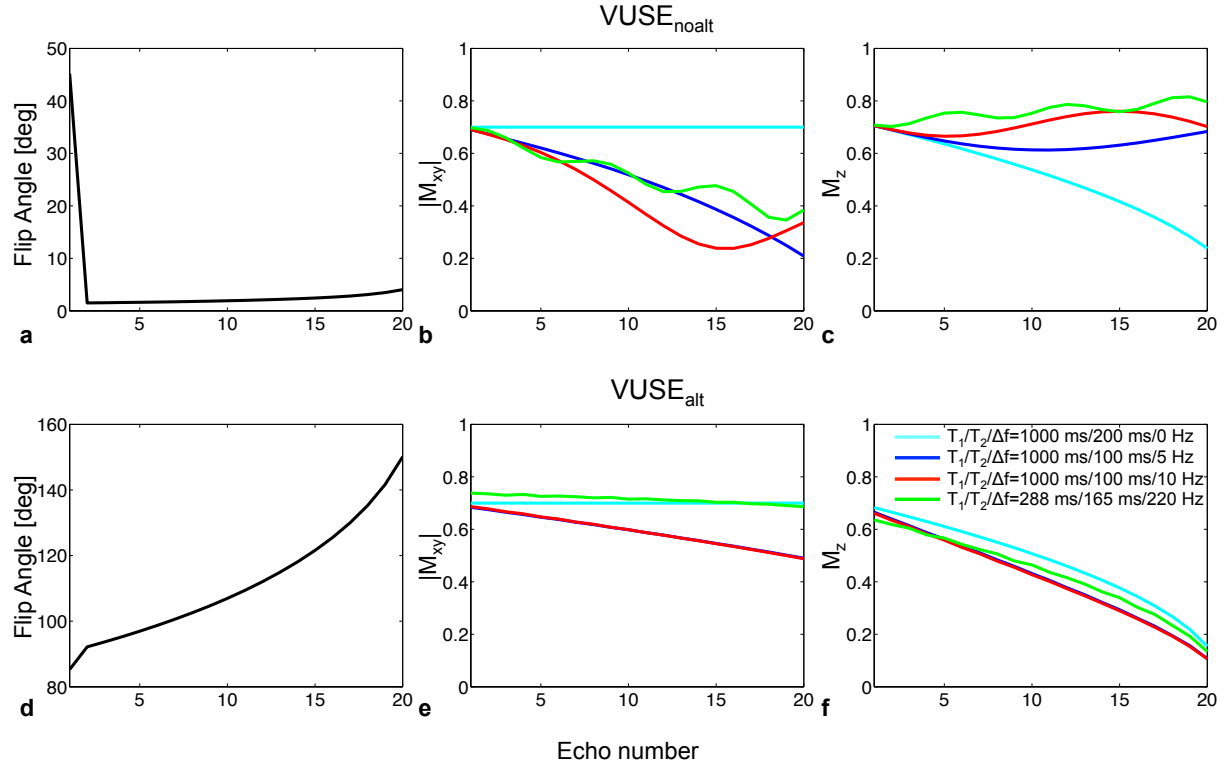


Figure 9.2: (a) VFA scheme of $VUSE_{noalt}$ required to maintain constant transverse magnetization of arterial blood (cyan). The simulation of the transverse (b) and longitudinal magnetization (c) of the venous blood with 5 Hz (blue), 10 Hz (red) and fat with off-resonance of 220 Hz shows the high sensitivity of the transverse magnetization to off-resonance. The VFA scheme of $VUSE_{alt}$ (d) increases with increasing FA approaching 180° to maintain constant arterial blood signal. The transverse magnetization (e) is not highly sensitive to off-resonance compared to $VUSE_{noalt}$ (blue and red curves). The longitudinal magnetization of all the tissues decrease with increasing echo number unlike $VUSE_{noalt}$.

Fig. 9.2a shows the simulated $VUSE_{noalt}$ scheme used to produce constant transverse magnetization (Fig 9.2b) of the arterial blood (cyan). The longitudinal magnetization (Fig 9.2c) of the arterial blood approaches zero with increasing echo number. Note that constant arterial blood transverse magnetization can be achieved with a very low flip angle scheme. However, $VUSE_{noalt}$ is very sensitive to off-resonance which is shown by the faster decay of the transverse magnetization of venous blood signal with 5Hz (blue), 10 Hz (red) and fat signal with 220 Hz (green) off-resonance (Fig. 9.2b) but the longitudinal magnetization of these tissues does not decay unlike the longitudinal magnetization of the arterial blood (Fig. 9.2c).

Fig. 9.2d shows that the FA scheme for $VUSE_{alt}$, with identical simulation parameters, increases with increasing echo number and approaches 180° to maintain constant transverse magnetization of the arterial blood by transferring signal from the longitudinal magnetization, which approaches zero. Unlike $VUSE_{noalt}$, the transverse magnetization (Fig. 9.2e) of the other tissues does not rapidly decay with echo number although they are sensitive to off-resonance. Note also that the longitudinal magnetization (Fig. 9.2f) of the other tissues decays similar to arterial blood in $VUSE_{alt}$ whereas they remain nearly constant in $VUSE_{noalt}$.

The frequency dependence of the transverse magnetization with echo number is shown in Fig. 9.3 for $VUSE_{noalt}$ and $VUSE_{alt}$. Fig. 9.3a clearly shows that the off-resonant venous blood signal decreases considerably with increasing echo number compared to $VUSE_{alt}$.

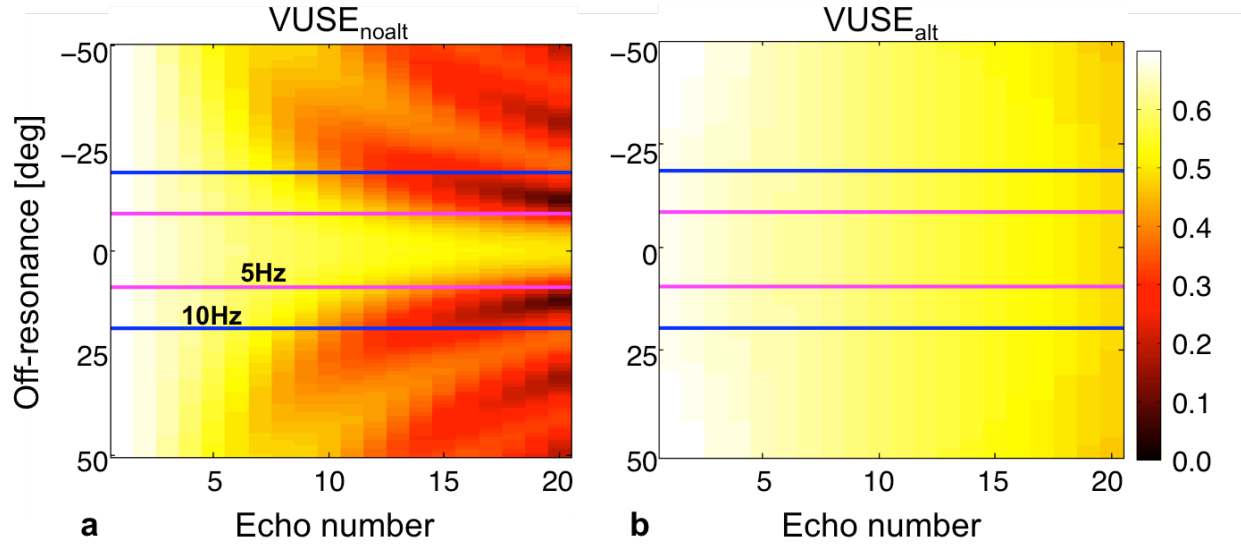


Figure 9.3: The frequency response of the venous blood ($T_1/T_2=1000/100$ ms) with the VFA scheme shown in Fig. 9.2. The signal considerably decreases with increasing echo number for off-resonant magnetization with $VUSE_{noalt}$ (a) compared to $VUSE_{alt}$ (b).

Fig. 9.4 shows a single slice of the lower leg acquired in a healthy subject with bSSFP, $VUSE_{alt}$, $VUSE_{noalt}$ and the maximum intensity projection (MIP) of the $VUSE_{noalt}$ images. The venous blood and the fat have a lower signal in $VUSE_{noalt}$ compared to $VUSE_{alt}$ due to off-resonance sensitivity and the lower T_2 (94) of the venous blood compared to arterial blood. Fig. 9.4d shows the MIP of the $VUSE_{noalt}$ images with clear depiction of the arteries. The deposited RF energy measured in Watt•seconds is indicated below each image and is $\sim 14\times$ times lower using $VUSE_{noalt}$ compared to bSSFP.

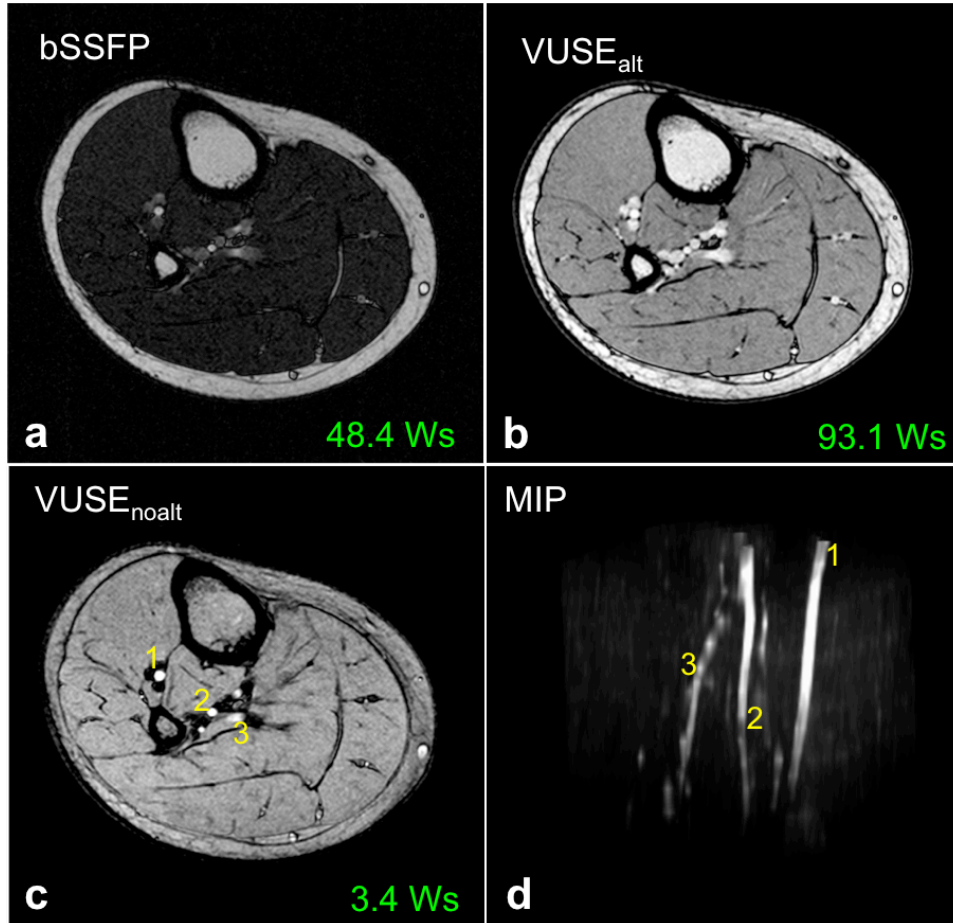


Figure 9.4: Single slice from a 2D multi-slice (a) bSSFP, (b) $VUSE_{alt}$, (c) $VUSE_{noalt}$ and (d) maximum intensity projection images of lower leg with the arteries labeled (1-anterior tibial artery, 2-posterior tibial artery, and 3-peroneal artery). Reduced venous blood and fat signal can be seen in $VUSE_{noalt}$. The RF energy deposited is indicated in green.

Fig. 9.5 shows single slice bSSFP, $VUSE_{alt}$, $VUSE_{noalt}$ and the maximum intensity projection (MIP) of $VUSE_{noalt}$ images acquired from another subject. Note that the venous blood signal is higher than in the first subject. The mean and standard deviation of the SNR measured in all the subjects in the different regions are shown in Table 9.1. $VUSE_{noalt}$ provides SNR comparable to bSSFP with much reduced SAR.

	bSSFP	VUSE _{alt}	VUSE _{noalt}
Arterial blood	28 ± 4	35 ± 5	32 ± 0
Venous blood	11 ± 1	32 ± 7	11 ± 11
Muscle	4 ± 0	21 ± 2	17 ± 0
Fat	22 ± 2	30 ± 8	16 ± 4

Table 9.1: SNR measured in arterial blood, venous blood, muscle, and fat for bSSFP, VUSE_{alt} and VUSE_{noalt} in three subjects.

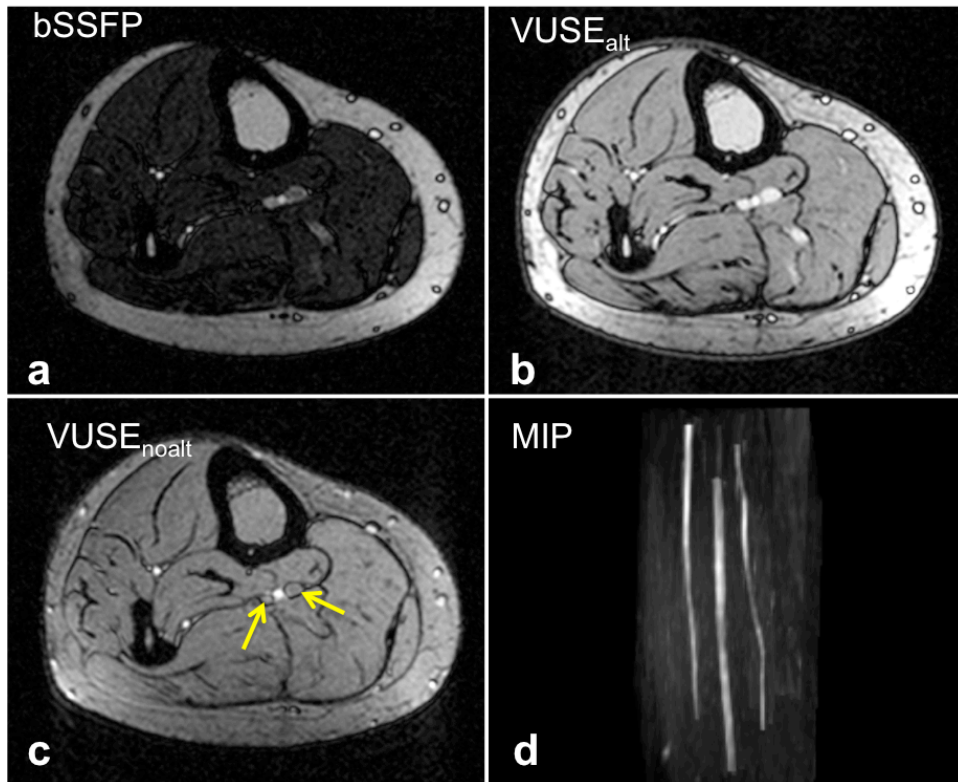


Figure 9.5: 2D a) bSSFP b) VUSE_{alt} c) VUSE_{noalt} and d) MIP of VUSE_{noalt} images of lower leg in another subject. Reduced venous blood and fat signal can be seen in VUSE_{noalt}. However, the venous signal was not as suppressed as in the subject shown in Figure 9.5 (yellow arrows).

9.6 DISCUSSION

Bloch simulations of the $VUSE_{noalt}$ scheme results in a very low FA scheme with high off-resonance sensitivity, which is useful for low SAR imaging applications as well as for high SNR off-resonance sensitive imaging applications like MR arteriography.

Both $VUSE_{alt}$ and $VUSE_{noalt}$ exhibit more T_2 -weighting as a consequence of transient-state imaging, which results in brighter muscle signal compared to steady-state bSSFP (Figs. 9.4-9.5). The magnitude of off-resonance in the venous and arterial blood signal is dependent on the blood oxygenation level as given by Eqn. 9.4. Hence, the venous signal will depend upon the individual's blood oxygenation, but will always be lower than the arterial blood signal. The contrast between the arterial and venous blood also depends on the k-space acquisition scheme. In Figs. 9.4-9.5, a linear segmented k-space acquisition was used. The k-space ordering may be changed to centric-out to improve the contrast between the arterial and venous signal. The differences in the blood oxygenation level will also change the T_2 of the venous blood and will result in similar signal changes between arterial and venous blood in both $VUSE_{noalt}$ and $VUSE_{alt}$.

The very low SAR property of $VUSE_{noalt}$ may be beneficial for ensuring the reduced heating of a device when scanning patients with implanted devices. The off-resonance sensitivity necessitates excellent shimming, but $VUSE_{noalt}$ can still be used to evaluate anatomy not immediately adjacent to the implant (e.g. head scan in a patient with a pacemaker). $VUSE_{noalt}$ may also be used for non-contrast MR arteriography owing to the bright arterial signal and inherent fat suppression.

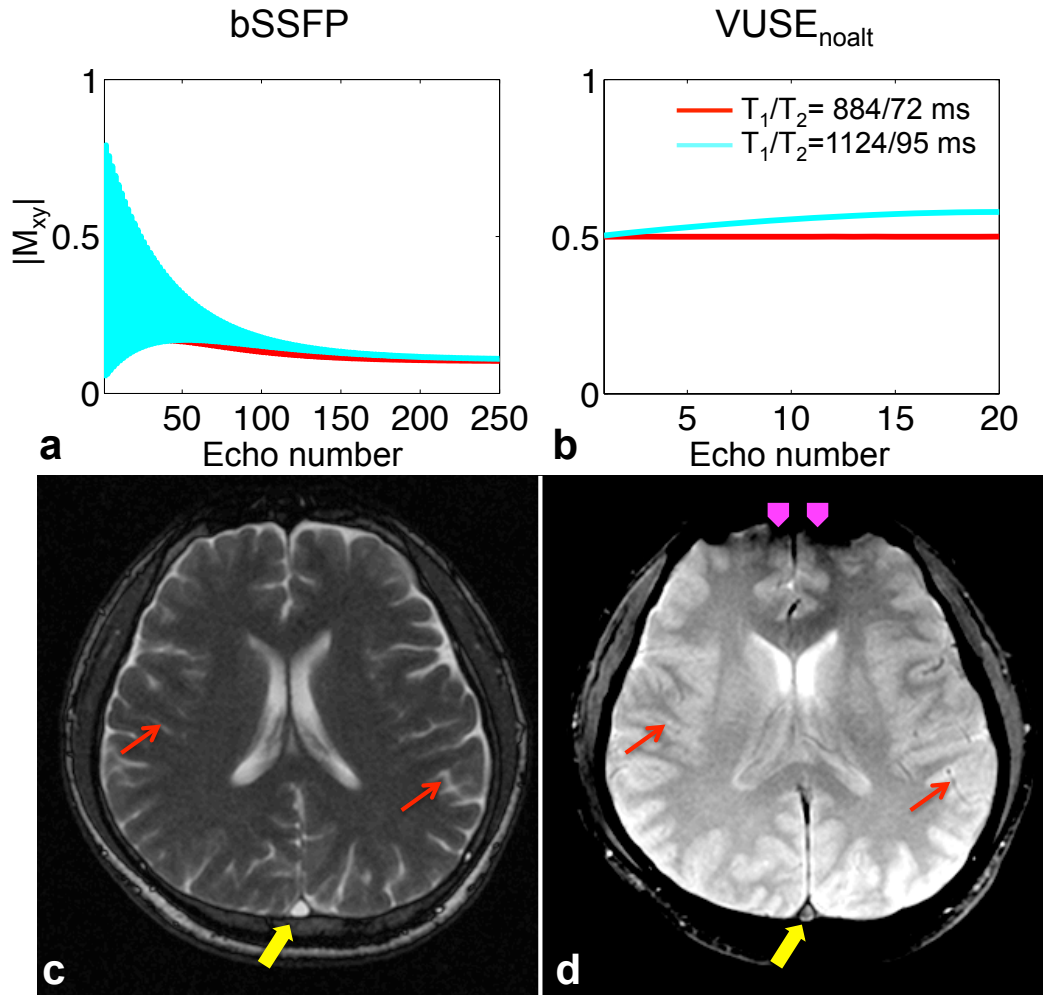


Figure 9.6: The simulation of the transverse magnetization of white matter ($T_1/T_2=884/72$ ms) and gray matter ($T_1/T_2=1124/95$ ms) for single-shot bSSFP (a) and segmented VUSE_{noalt}. The steady-state bSSFP signal has poor white matter and gray matter contrast that is improved in VUSE_{noalt} due to transient imaging. 2D (c) single-shot bSSFP, (d) segmented VUSE_{noalt} images of the brain showing bright arterial and venous blood in bSSFP. Both the sinus (yellow arrow) and the other veins (red arrows) have a lower signal with VUSE_{noalt} compared to bSSFP. Pronounced off-resonance artifacts, however, can be seen in VUSE_{noalt} (magenta arrow heads).

VUSE_{noalt} can also be used to explore other applications that may benefit from the contrast between arterial and venous blood. Fig. 9.6a-b shows the simulation of gray matter and white matter for single shot bSSFP and VUSE_{noalt}. 2D multi-slice interleaved segmented acquisition of the brain acquired with single-shot bSSFP compared to VUSE_{noalt} acquisition is shown in Fig 9.6c-d. Note that the venous signal appears dark in the VUSE_{noalt} compared to bSSFP (red arrows, yellow arrow) with strong T₂ weighting.

Limitations

The constant transverse magnetization is maintained by transferring more longitudinal magnetization to the transverse plane and hence the longitudinal magnetization approaches zero with increasing echo number. Hence, when the longitudinal magnetization approaches zero, there must be a delay to allow for complete signal recovery before subsequent acquisition. Due to the high sensitivity of VUSE_{noalt} to off-resonance, even the on-resonant signal will dephase with increasing echo number. Hence, interleaved segmented images were acquired with high M_T of 0.7. However, segmented acquisitions require longer acquisition durations especially for 3D imaging.

9.7 CONCLUSION

VUSE_{noalt} can be used for high SNR, low SAR MR arteriography and other off-resonance sensitive imaging applications with constant transverse magnetization. VUSE_{noalt} reduces the venous blood signal by a factor of ~3 compared to the arterial blood with lower fat signal.

9.8 APPENDIX

The flip angle required to maintain constant transverse magnetization can be derived using Bloch simulations. When an RF pulse with a flip angle α is applied along the x-axis, the magnetization rotates along the x-axis, which can be represented in matrix form as follows:

$$R_{\alpha} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos \alpha & \sin \alpha \\ 0 & -\sin \alpha & \cos \alpha \end{bmatrix}.$$

The free precession with T_2 decay and T_1 relaxation can be expressed as $A M + B$ where

$$A = \begin{bmatrix} e_2 & 0 & 0 \\ 0 & e_2 & 0 \\ 0 & 0 & e_1 \end{bmatrix}, B = \begin{bmatrix} 0 \\ 0 \\ (1 - e_1)M_0 \end{bmatrix} \text{ and } e_{1,2} = e^{\left(-\frac{TE}{T_{1,2}}\right)}.$$

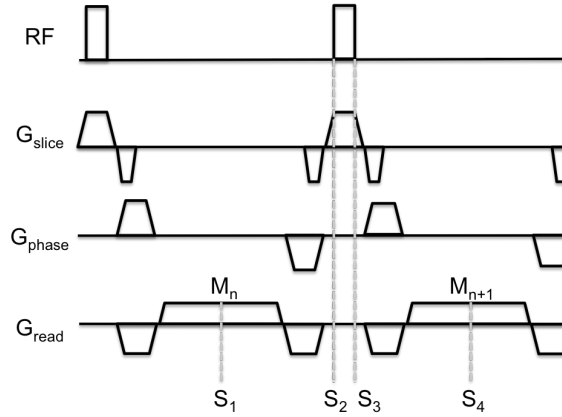


Fig. 9.8.1 Pulse sequence diagram of the bSSFP showing the time points at which the signal is being calculated.

The signal at time points 2, 3, and 4 in Fig. 9.8.1 are given by

$$S_2 = A M_n + B \quad [9.8.1]$$

$$S_3 = R_{\alpha} S_2 \quad [9.8.2]$$

$$S_4 = M_{n+1} = A S_3 + B \quad [9.8.3]$$

Eqn. 9.8.3 can be re-arranged to solve for R_{α} as $A^{-1}(M_{n+1} - B) = R_{\alpha} A M_n + R_{\alpha} B$

Let $G = \begin{bmatrix} G_1 \\ G_2 \\ G_3 \end{bmatrix} = A M_n + B$ and $M_{n+1} = \begin{bmatrix} 0 \\ M_T \\ M_z \end{bmatrix}$ where M_T is the desired constant transverse

magnetization. Substituting the above equation with $A_{22}^{-1} = 1/e_2$ into the y-component of Eqn.

9.8.3 gives

$$\frac{M_T}{e_2} = H = G_2 \cos \alpha + G_3 \sin \alpha \quad [9.8.4]$$

where $G_2 = e_2 M_{xy}$; and $G_3 = e_1 M_z + (1 - e_1) M_0$.

Dividing Eqn. 9.8.4 with $\cos \alpha$ on both sides results in

$$H \sec \alpha = G_2 + G_3 \tan \alpha \quad [9.8.5]$$

The desired flip angle can be derived by squaring Eqn. 9.8.5 and solving for $\tan \alpha$ as follows:

$$\begin{aligned} H^2(1 + \tan^2 \alpha) &= G_2^2 + G_3^2 \tan^2 \alpha + 2 G_2 G_3 \tan \alpha \\ (H^2 - G_3^2) \tan^2 \alpha - 2 G_2 G_3 \tan \alpha + (H^2 - G_2^2) &= 0 \\ \tan \alpha &= \frac{2 G_2 G_3 \pm \sqrt{(2 G_2 G_3)^2 - 4(H^2 - G_3^2)(H^2 - G_2^2)}}{2(H^2 - G_3^2)} \end{aligned} \quad [9.8.6]$$

CHAPTER 10

CONCLUSION

bSSFP cardiac cine imaging is clinically preferred due to its improved blood-myocardium contrast. Detailed Bloch simulations of stationary myocardium and flowing blood that account for the imperfect slice profile and off-resonance effects can be used to determine the optimal flip angle required for high contrast cardiac cine imaging. In vivo imaging in healthy subjects and clinical patients showed that high blood-myocardium contrast can be obtained with a FA $\sim 105^\circ$ when imaging a plane with predominantly through-plane flow such as the short-axis plane. However, if through-plane flow is limited, as may occur for patients with low ejection fraction or low heart rates or in the long axis imaging planes wherein in-plane flow is present, then the FA should be limited to $\sim 75^\circ$ for best contrast. This work, titled “Optimal Flip Angle for high contrast balanced SSFP cardiac cine imaging” has been published in *Magnetic Resonance in Medicine*, 2014; doi: 10.1002/mrm.25228.

The VFA-bSSFP technique can be used to lower the SAR and maintain the blood-myocardium contrast, which is useful for safe and improved patient comfort as well as enabling imaging at higher field strengths with better image contrast. An asynchronous k-space acquisition was proposed to enable cardiac cine imaging with VFA-bSSFP. This novel asynchronous VFA-bSSFP technique can be used to lower the SAR by at least 36% with similar blood-myocardium CNR compared to the conventional bSSFP cardiac cine imaging. Asynchronous VFA-bSSFP can also be used to increase the CNR by at least 28%, with similar SAR compared to conventional bSSFP. This work, titled “Variable flip angle balanced steady-state free precession for lower SAR or higher contrast cardiac cine imaging” has been published in *Magnetic Resonance in Medicine*, 2014; 71(3): 1035-1043. A US patent application has also been submitted for this work.

aVFA-bSSFP has also been applied for free-breathing, bellows gated, cardiac cine imaging at 3T for low SAR imaging and reduced patient discomfort. The optimal VFA scheme that

maximizes the SAR reduction with blood-myocardium contrast similar to constant flip angle cardiac cine imaging was determined using Bloch simulations. aVFA-bSSFP reduced the SAR by at least ~25% for free-breathing cardiac cine imaging compared to conventional breath-hold acquisition (BH CFA) with similar blood-myocardium contrast and with image quality sufficient to perform global and regional cardiac function analysis. This work, titled 'Free breathing low SAR cardiac cine balanced SSFP Imaging at 3T' is in preparation for journal submission.

Future work could evaluate similar asynchronous VFA-bSSFP schemes for high spatial and temporal resolution of cardiac cine imaging in patients with arrhythmias where conventional segmented approaches cannot be used for cardiac cine imaging. aVFA-bSSFP can also be used for other cardiac cine applications such as phase contrast imaging, or other physiological signal retro-gated acquisitions. Alternately, aVFA-bSSFP can be used for improved contrast 3D cardiac cine applications compared to similar SAR conventional 3D cardiac cine approaches due to the ability to use a higher imaging flip angle.

Variable flip angle imaging can also be used for several other applications. For example, clinical 3D T_2 weighted imaging is commonly performed using 3D FSE techniques, which require longer acquisition durations ~7min for 3D prostate imaging thereby increasing the susceptibility of motion artifacts. We have developed a 3D T_2 -TIDE bSSFP imaging technique at 3T with the following features: 1) the T_2 weighted signal is obtained by imaging during the transient bSSFP state enabling increased echo train duration; 2) VFA scheme is used to reduce the SAR at 3T and hence enable the use of higher signal for improved contrast; 3) the interleaved spiral-out phase encode ordering in the k_y - k_z plane enables fast acquisition of 3D k -space, limits spatial-resolution losses, and reduces the acquisition duration by ~58% compared to 3D FSE with identical imaging parameters and higher SNR efficiency. This work, titled "Fast Three-Dimensional T_2 -weighted Imaging with Transition Into Driven Equilibrium balanced SSFP at 3T" is in review for journal publication to Magnetic Resonance in Medicine. A provisional US patent has been applied for this work.

Moving forward the 3D T_2 -TIDE technique could be used for 3D T_2 weighted imaging of the brain, breast, abdominal and other body MRI for fast imaging at 3T. Notably, a multi-slab approach may be especially useful for breast imaging wherein two slabs could be acquired in the same acquisition time by imaging one slab during the magnetization recovery interval of the other slab. The 3D T_2 -TIDE also enables control of the acquisition duration, albeit at the cost of image sharpness, which may be useful for fast 3D T_2 weighted imaging during interventional procedures. Other 3D T_2 -weighted approaches have hard limits on the minimum acquisition time that make them unsuitable for real time imaging.

Another application of VFA bSSFP imaging is in non-contrast enhanced MR arteriography. The VFA scheme used to generate constant transverse magnetization with the bSSFP sequence without using RF phase alternation ($VUSE_{noalt}$), is sensitive to off-resonance and was applied for high SNR, non-contrast enhanced MR arteriography of the lower leg. $VUSE_{noalt}$ reduces the venous blood signal by a factor of about three-fold compared to the arterial blood with reduced fat signal. This work, titled 'Very low SAR imaging of the lower leg using variable angle for uniform signal excitation (VUSE) and balanced SSFP without RF phase cycling' was presented at ISMRM, Melbourne, 2012, abstract: 2500.

The off-resonance property of this sequence may also be used for other applications such as functional imaging. Real-time applications of the $VUSE_{noalt}$ sequence may be performed using parallel imaging techniques, compressed sensing or with modified k-space trajectory.

Overall, VFA-bSSFP is a promising technique that can be further explored for low SAR or improved signal imaging at higher field strengths. These techniques can also be optimized for other SSFP imaging techniques like FISP and PSIF applications in stationary regions.

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