

SEQUENCE DESIGN AND CONTRAST OPTIMIZATION

SEQUENCE DESIGN AND CONTRAST
OPTIMIZATION OF SUSCEPTIBILITY
WEIGHTED IMAGING

By
YINGBIAO XU, B.S, M.S
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AUTHOR: Yingbiao Xu
B.S. (Geophysics),
M.S. (Geophysics)
University of Science & Technology of China
M.S. (Computer Science)
Washington University in St. Louis

SUPERVISOR: E.Mark Haacke, Professor Max Wong,
Professor

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Dedications
To my family

Abstract

Susceptibility Weighted Imaging (SWI) utilizes the susceptibility difference between tissues to create a new type of imaging contrast in MRI that is different from conventional spin density, T1-, or T2-weighted imaging. The SWI sequence is a high resolution, fully flow compensated gradient echo sequence. High resolution reduces the signal loss caused by local field inhomogeneities yet with relatively long echo time sufficient contrast can be generated between tissues with a susceptibility difference. Contrast between tissues in the phase image is directly proportional to the susceptibility difference and can be used to enhance the contrast in the magnitude image. In this thesis, we optimize the contrast to noise ratio (CNR) in the magnitude image as a function of the multiplication of the phase mask generated from the phase image. We find that a shorter echo time has the advantage of achieving higher CNR efficiency compared with longer echo times. SWI has found numerous clinical applications due to its sensitivity to blood products. Partial volume effects occur when a voxel contains both venous blood and brain parenchyma. We studied the apparent phase of a voxel as a function of imaging resolution and predict what the best imaging parameters for a specific clinical application should be. Currently, a long acquisition time is the bottleneck for SWI to be used as a routine protocol in the clinical environment. This thesis evaluates segmented echo planar imaging (SEPI) as an alternative to speed up the acquisition while reducing the artifacts usually associated with other fast imaging methods.

Executive summary

Susceptibility Weighted Imaging (SWI) has numerous clinical applications including imaging tumors, trauma, stroke, occult vascular disease, and a variety of other neuro-vascular diseases such as vascular dementia, cerebral amyloid angiopathy, and sturge-webber disease due to its capability to image veins [10], [12], [15], [37-38], [42]. High resolution phase images which come part and parcel with SWI allow researchers to study anatomical structures of the mid-brain and basal ganglia and can be used for iron quantification [11]. The conventional SWI sequence is a 3D high resolution, fully flow compensated (in all three directions) gradient echo sequence. A sufficiently long echo time has to be applied to achieve susceptibility weighting (or T_2^* -weighting). In Susceptibility Weighted Imaging, phase images play an important role in the production of susceptibility-weighted (SW) contrast [9]. Phase images also give excellent contrast between anatomical structures. In previous studies [34-35], [45], the phase images are high-pass filtered and then transformed to a special ramp-like phase mask with values ranging from zero to unity. This phase mask is then multiplied a few times into the original magnitude image to enhance the contrast to noise ratio (CNR) of the magnitude image. The question that remains to be answered is how to optimize the process to get the optimal CNR of the magnitude image between venous vessels and brain parenchyma. In this thesis, we simulate how CNR of the magnitude image between venous vessels and brain parenchyma

varies with the phase difference and number of times the phase mask multiplication is applied. The result allows us to better understand how to enhance the CNR in terms of the concept of constant imaging time. Shorter echo times have the advantage of achieving higher $\text{CNR}/\sqrt{\text{time}}$ compared with longer echo times. Plus shorter echo times make it less likely for phase to alias at the edge of a vessel, which could cause a vessel to appear fatter than it actually is when phase masking is applied. In terms of imaging efficiency, a shorter echo time allows for a larger volume coverage, which is desirable in a clinical environment.

The apparent phase of a voxel suffers from a partial volume effect when a voxel contains both a venous vessel and background brain parenchyma. The apparent phase of a voxel also depends on the vessel orientation relative to the B_0 field. It's important to understand the partial volume effect due to SWI's wide variety of clinical applications. In this thesis, we model the vein as an infinitely long cylinder perpendicular to the main magnetic field. The results show how the apparent phase of a voxel in the image changes as a function of resolution, vessel size and, to a lesser degree, vessel center within the voxel. The simulations explain why a negative-phase mask has worked in SWI processing of high-resolution images collected in the transverse direction, despite the expected positive-phase behavior for vessels perpendicular to the main field. Now with the

understanding of the partial volume effect, we can predict the optimal echo time and resolution in terms of the size of the vessel under investigation.

High resolution and long echo times lead to a long imaging time. For example, to cover 32 slices with $0.5 \times 1.0 \times 2.0 \text{ mm}^3$ resolution on a 1.5T system takes more than 8 minutes. To cover the whole brain, which is desired not only from a clinical point of view but also for post processing to remove background phase, will double the scan time to 16 minutes and is practically not feasible in a clinical environment. At high field such as 7T, high SNR allows to push the resolution to $0.25 \times 0.25 \times 0.5 \text{ mm}^3$ which leads to even higher constraints on imaging speed. In a clinical environment, long acquisition time is a concern for patient comfort, clinical throughput, and to leave time apply other imaging methods. Too long a scan time could be the main roadblock for SWI to be a routine neuro-imaging protocol. To speed up the SWI acquisition, in this thesis, an alternate approach using a gradient echo segmented EPI sequence is investigated to achieve similar susceptibility-weighting compared to a conventional gradient echo SWI sequence. Efforts are made to minimize the common artifacts associated with an EPI sequence namely distortion and ghosting. However, one major drawback with this segmented EPI approach is that both arterial and venous signals become dark while the conventional SW image has bright arterial signal and dark venous signal. The natural separation of arterial and venous signals could be important if the venous structure is the point of

interest. A center out k-space trajectory could bring back the arterial signal loss [1] while the distortion would be doubled with the current echo time shifting (ETS) [5] technique. In this thesis, a new sequence namely Geometric Distortion Corrected Segmented EPI (GDC-SEPI) is designed to overcome the drawbacks (dark arterial signal and distortion) related to conventional segmented EPI technique. GDC-SEPI utilizes a center out k-space trajectory and an iterative phase correction technique to remove the phase discontinuities between segments hence reducing the distortion. Numerical simulations show the good potential of the GDC-SEPI sequence while the real acquisition of the sequence shows residual artifacts likely due to the imperfect phase estimation.

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List of Acronyms and Notations

2D	two-Dimensional
3D	three-Dimensional
B_0	Main magnetic field strength
$\vec{B}$	Magnetic field
BOLD	Blood Oxygen Level Dependent
CNR	Contrast to Noise Ratio
CPR	Conjugate phase reconstruction
EPI	Echo Planar Imaging
ETS	Echo time shift
fMRI	Functional MRI
GDC-SEPI	Geometric Distortion Corrected Segmented EPI
GRAPPA	Generalized Auto-calibrating Partially Parallel Acquisition
GRE	Gradient recalled echo
GM	Gray matter
FLASH	Fast low angle shot
FSE	Fast spin echo
$\vec{H}$	Field defined as $\vec{B}/\mu_0 - \vec{M}$
Hct	The fractional hematocrit
mIP	Minimum intensity projection

$\vec{M}$	Magnetization
MR	Magnetic Resonance
MRA	Magnetic Resonance angiography
MRI	Magnetic Resonance Imaging
MRM	Magnetic Resonance in Medicine
N_{rf}	Index of RF pulses
N_x, N_y	Points collected along the x and y direction
PE	Phase encoding
ppm	Part per million
PRESTO	Principle of echo shifting with a train of observations
RF	Radio frequency
ROI	Region of interest
SD	Standard deviation
SENSE	Sensitivity Encoding
SEPI	Segmented Echo Planar Imaging
SNR	Signal to Noise Ratio
sqrt	Square root operator
SW	Susceptibility-weighted
SWI	Susceptibility Weighted Imaging
T1	Spin-lattice relaxation time
T2	Spin-spin relaxation time
T2*	Effective transverse relaxation decay

T	Tesla. Magnetic field unit
T_E	Echo time
TE	Echo time
TR	Repetition time
TSE	Turbo spin echo
TSF	Turbo segmented factor
WM	White matter
ρ	Spin density
χ_{do}	Susceptibility difference between fully deoxygenated blood and fully oxygenated blood
ΔB	Field inhomogeneity
$\Delta k_x, \Delta k_y$	Sampling interval along k_x and k_y direction
ΔT	The inter-echo time interval in an echo train
γ	Gyromagnetic ratio of protons
φ	Spin phase
σ	Standard deviation
$*$	Multiplication operator
μ_0	Permeability of empty space

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Chapter 1

Introduction

Overview to Susceptibility Weighted Imaging

History

Functional brain imaging is an exciting area of research in magnetic resonance imaging (MRI) (for general reviews of how MRI works see references [13],[19],[30],[43]). This field began in the early 90's with the ground breaking work of Ogawa et al [27-29] which showed that T2*-weighted images of human subjects were sensitive to the changes in cerebral blood flow due to sensory and motor stimulation. The work demonstrated that the main mechanism of contrast change is through change in blood oxygenation level. Since then blood oxygen level dependent (BOLD) contrast has been one of the main mechanisms for brain functional MRI (fMRI) studies. However, the early explanation for the method involved diffusion effects to explain signal loss. Haacke et al proposed that the source was from bulk magnetic susceptibility effect in the veins [8], [17]. The paramagnetic deoxyhemoglobin in venous blood generates local magnetic field inhomogeneities. In 1982, Thulborn et al observed T2* shortening of venous blood. There is a bulk volume susceptibility difference of 0.18 ppm between deoxygenated red blood cells and surrounding plasma [41]. Hence deoxyhemoglobin can be used as a contrast agent for venous visualization [34].

The bulk susceptibility difference also results in a phase difference between a vessel and its surroundings [27]. The phase difference is a function of echo time. In a simple two-compartment model, an echo time can be so chosen to maximize the signal cancellation effect. Both $T2^*$ shortening and phase shift between venous blood and its surrounding are the bases for BOLD contrast.

The “susceptibility-weighted” imaging in MRI generally refers to the technique used for improving the sensitivity to the susceptibility effects. In 1990, Rosen et al [36] used susceptibility-weighted magnitude image with bolus injection of paramagnetic contrast agents to assess the cerebral perfusion. In 1992, Conturo et al [3] proposed phase-angle reconstruction to measure the phase shift caused by the paramagnetic contrast agent. In 1993, Crespigny et al [4] compared the real image which combines the information of both the intensity of the magnitude and the phase angle with the magnitude image to see the improved sensitivity to the susceptibility contrast.

For susceptibility contrast, a gradient recalled echo (GRE) sequence or its variant is the choice in MRI. Crespigny et al [4] used a FLASH sequence in their study. In 1997, Reichenbach et al [34] developed a fully velocity compensated 3D high resolution GRE sequence for MR venography. The work also creates a phase mask from the phase image and multiplies the mask multiple times to the magnitude image to enhance the contrast in the magnitude image. The sequence is

later referred to as the SWI sequence. Today parallel imaging techniques are used routinely to reduce the scan time. In 2004, Haacke et al [9] formally introduced Susceptibility Weighted Imaging (SWI) after optimizing the acquisition and post processing. In 1992, Moonen et al [24] developed an echo-shifted GRE sequence to improve the sensitivity to the dynamic susceptibility effects. The technique allows the same imaging scan time while push the echo time (TE) longer than the repeat time (TR). In 1993, Liu et al [22] developed a technique combining Principles of Echo-shifting with a train of Observations (PRESTO). The technique used an echo-shifting technique while acquiring multiple k-space lines within a single TR. PRESTO was further combined with the SENSE technique for rapid susceptibility-weighted 3D MRI time series in 2003 [16]. PRESTO is more used in whole brain functional imaging to improve the temporal resolution. Another type of sequence used for susceptibility-weighted imaging is segmented Echo Planar Imaging (EPI) [18], [21].

Motivation

Susceptibility Weighted Imaging (SWI) has numerous clinical applications including imaging tumors, trauma, stroke, occult vascular disease, and a variety of other neuro-vascular diseases such as vascular dementia, cerebral amyloid angiopathy, and sturge-webber disease due to its capability to image veins [10], [12], [15], [37-38], [42]. It's important to have a complete understanding of the contrast behavior of SWI before it becomes part of routine neuro-vascular

imaging protocol in clinical environment. One of the two main goals in this thesis is to optimize the SWI acquisition and post processing for different clinical applications. The other is to improve the acquisition speed while minimizing the artifacts. With the SWI sequence, acquisition time for whole brain coverage combining with 3D high resolution results in an excessively long acquisition time. High resolution is crucial to detect microhemorrhages, shearing and diffuse axonal injury in trauma patients. High resolution might also lead to early detection of tumor angiogenesis. There is increasing evidence that several neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, are associated with altered brain iron metabolism. For many years the iron distribution in the human brain could be studied effectively only under postmortem conditions. Now the situation is changed. High resolution phase images which come part and parcel with SWI allow researchers to study anatomical structures of the mid-brain and basal ganglia and can be used for iron quantification [11]. High resolution SWI might detect changes in brain iron concentrations associated with disease states and suggest that iron-dependent MR imaging may soon provide biomarkers capable of characterizing the presence and progression of important neurological disorders. Such biomarkers may be of crucial assistance in the development and utilization of effective new therapies for Alzheimer's disease, Parkinson's disease and multiple sclerosis.

Mechanism

In a gradient echo sequence, a relatively long echo time creates a T2*-weighted (or susceptibility weighted) image to show local susceptibility effects [33]. While the T2* BOLD effect has been the main mechanism for the brain functional imaging studies, it has also been applied to high resolution MR venography to visualize veins in detail [34-35]. In the simplest perspective, when it comes to imaging veins, a long echo time creates a T2*-weighted contrast and allows a natural separation between arterial signal and venous signal [45].

To understand the mechanism of venous visualization in SWI, a two-compartment model (a voxel consisting of venous blood and background brain parenchyma) may be used. First when there is a field inhomogeneity, the spin phase, ϕ , for a right handed system, develops according to the simple linear formula

$$\phi = -\gamma\Delta B T_E \quad (1)$$

where γ is the gyromagnetic ratio of protons, ΔB is the field inhomogeneity, and T_E is the time at which the data are sampled after the excitatory radiofrequency pulse is applied. The simple linear relationship of spin phase with T_E assumes no partial volume effect, i.e., there is only one type of tissue or the resolution is infinity. For a venous vessel with an arbitrary angle θ to the main field, both intra-vascular and extra-vascular inhomogeneities develop. Consider an infinitely long cylindrical-like vessel. Infinite length makes it a two dimensional problem

with the boundary conditions of both the normal component (radial) of $\vec{B}$ field and tangential component of $\vec{H}$ field continuous at the boundary of the cylinder. By solving Maxwell's equation with the above boundary conditions, we get the intra-vascular and extra-vascular fields. For the intra-vascular field, the magnetic field difference ΔB_{in} can be written as [7],[32]

$$\Delta B_{in} = 4\pi\chi_{do} (3\cos^2\theta - 1) B_0(1-Y)Hct / 6 \quad (2)$$

χ_{do} is the difference in susceptibility of fully deoxygenated blood and fully oxygenated blood (this term has been evaluated to be 0.18 ppm by Weisskoff et al [46]); Y is the oxygen saturation, Hct is the fractional hematocrit and B_0 is the main static field strength. For the extra-vascular field, the field difference ΔB_{out} can be written as

$$\Delta B_{out} = 4\pi\chi_{do} \sin^2\theta \cos 2\phi (r^2/\rho^2) B_0(1-Y)Hct/2 \quad (3)$$

where ϕ is the angle between the main field and the projection of the position vector onto the plane perpendicular to the long axis of the vessel, r is the radius of the vessel and ρ is the distance of the position P to the center of the vessel. The final MR signal of the voxel can be evaluated with numerical integration of signal within the voxel. Generally both intravascular field and extravascular field cause signal cancellation and helps create contrast between background tissue and sub-voxel veins.

For a special case when the vessel is parallel to the main field, the extravascular field is zero. Taking $B_0 = 1.5\text{T}$, using $Y = 0.55$ for Weisskoff's results, $Hct = 0.45$, and $\gamma = 2\pi(42.58)\text{ MHz/T}$ yields [46]

$$\phi = -20\pi T_E \quad (4)$$

where ϕ is in radians when T_E is given in milliseconds. When $T_E = 50\text{ms}$, $\phi = -\pi$.

If the vein in question occupies the same voxel as the parenchyma (i.e., there is partial volume of vein and background tissue) then the signal of the venous blood opposes that of the background tissue and leads to maximum signal cancellation. The final apparent phase of the voxel could be either zero or $-\pi$ depending on the volume fraction of the venous vessel. The estimated echo time for which the phase of the venous blood reaches $-\pi$ also varies with the estimated oxygenation level. In practice, a TE of 40 ms (1.5T), 20 ms (3T) and 15 ms (4T) are selected so that the phase is invariant in different field strength. While those echo times might not be optimal, they produce quality SWI images.

A high-resolution 3D gradient echo sequence with full flow compensation in all three directions (readout, phase encoding, and slice select) is used in MR venographic imaging [34] or more generally susceptibility weighted imaging [9]. Fully velocity compensated in all three directions ensures that there is no vessel misregistration and no accumulation of phase due to motion leaving just phase from local changes in tissue susceptibility. Thin slices reduce the signal losses where large static field inhomogeneities are present [33]. In-plane high resolution

enhances the partial volume effect or signal cancellation effect between small veins and background brain parenchyma. In addition to the $T2^*$ contrast available in the magnitude image, the novel idea in this method is the generation of magnitude contrast from the phase image. To enhance the magnitude contrast with phase data, first a high-pass filter is applied to phase image to remove the low spatial frequency components of the background local field [33], [45]. Second, the filtered phase image is used to create a phase mask by applying a ramp-like filter to the phase image itself. Then the phase mask is used to multiply the original magnitude image about four times to enhance the contrast in the magnitude image. Finally, a minimum intensity projection (mIP) is performed over a number of slices to view the connectivity of the venous vessels.

In summary, the combination of the following features defines Susceptibility-Weighted Imaging (SWI): high resolution 3D gradient echo imaging (which reduces the signal loss due to unwanted background field inhomogeneities while increasing the signal cancellation effect for sub-voxel veins); full velocity compensation in all three directions (readout, phase encoding and slice select); high-pass filtering to the phase image (to remove unwanted background phase information); unique creation of a phase mask (to highlight certain susceptibility properties); multiplication of the phase mask into the magnitude images (to create a susceptibility weighted image); and finally taking a minimum intensity projection to view vessel connectivity [34]. In other words,

Susceptibility-Weighted Imaging (SWI) is indeed a $T2^*$ -weighted mechanism. However, SWI is not just simply a $T2^*$ contrast. Proper selection of the sequence protocol including echo time, resolution and flip angle is the key to SWI imaging by taking into account the signal cancellation effect, $T2^*$ contrast and optimal post phase processing to enhance CNR of the magnitude image.

Contrast Optimization

One of the goals of this thesis is to adjust the phase processing to obtain optimal CNR of the SWI image between venous vessels and brain parenchyma. To address this goal, we simulate how CNR of the SWI image between venous vessels and brain parenchyma varies with the phase difference of the tissues and number of phase mask multiplications. Flip angle is selected in such a way that we have a relatively flat $T1$ contrast to begin with. Leaving out the partial volume effect and $T2^*$ contrast, we look at how CNR is generated by multiplication of phase mask into the magnitude image. First we investigate how CNR varies with number of phase mask multiplications for a series of phase differences between two types of tissues for fixed SNR. This allows us to estimate the optimal number of phase mask multiplication for different phase values. Obviously, the phase discrepancy between two types of tissues is a function of echo time and hence the acquisition time. It's more realistic to look at how $CNR/\sqrt{\text{time}}$ changes as a function of the number of phase mask multiplications rather than CNR itself, i.e., to look at the problem from an imaging efficiency point of view. For example,

doubling the echo time will roughly double both the scan time and phase difference. The question to ask is which approach is better: double the echo time or run the same echo time twice then average them to boost the SNR? With the signal loss from $T2^*$ effect, it's not hard to guess that shorter echo time has the advantage of achieving higher $CNR/\sqrt{\text{time}}$ compared with excessively long echo times. Further, a shorter echo time makes it less likely for phase to alias at the edge of a vessel, which can create a fatter vessel when the phase mask is applied. In terms of imaging efficiency, a shorter echo time also make it possible to cover a larger volume, which is strongly desired in a clinical environment. However, partial volume effects must be taken into account before the optimal phase difference between venous blood and the brain parenchyma can be translated to an optimal echo time.

Partial volume effect

Ironically, the partial volume effect of small veins and tissue is an important aspect of SWI imaging. Specifically partial volume effect causes a signal cancellation between venous blood and brain parenchyma. The apparent phase of a voxel also suffers from partial volume effect when a voxel contains both vein and background brain parenchyma. While both intravascular and extravascular fields depend on the vessel orientation relative to the B_0 field, the apparent phase of the voxel is a function of vessel aspect ratio as well. For example, we observe negative phase for the veins perpendicular to the field in transverse acquisition

while the same vein could appear with a positive phase on sagittal acquisition. It's easy to understand that when the vessel is parallel to the main field, the maximum cancellation comes when the phases of venous blood and brain parenchyma lie in opposite directions. If the signal fraction of the venous blood is equal to that of the brain parenchyma, the CNR is optimal. This is not the case for vessels at an arbitrary angle along the main field. In this thesis, we model the vein as an infinitely long cylinder perpendicular to the main magnetic field (most of the lateral cervical veins appear nearly perpendicular to the field). We look at how the apparent phase of a voxel in the image changes as a function of resolution, vessel size and, imaging orientation. One question to bear in mind is "Why has a negative-phase mask worked so well in SWI processing of high-resolution images collected in the transverse direction, despite the expected positive-phase behavior for vessels perpendicular to the main field?" We also look at how the CNR of an SWI image changes as a function of resolution. Simulations show that the maximum cancellation might not create the optimal CNR for the final SWI image in some cases. With a better understanding of the partial volume effect, we could predict the optimal echo time and resolution in terms of the size of vessel to investigate.

Fast Imaging

The long scan time required for high resolution imaging is the main roadblock for SWI as a routine neuro-imaging protocol. There is a multitude of fast imaging

techniques to speed up the imaging acquisition for different circumstances. Parallel imaging techniques offer at least reduction of 2 in scan time. In practice, the GRAPPA [6] technique has less image artifacts especially aliasing than SENSE [31] technique. A higher reduction factor in scan time not only results in a greater SNR loss but also more artifacts. Parallel imaging requires multi-channel coils to reduce the gradient encoding steps with the information provided by the spatial dependent coil sensitivity. Today the multi-channel coil is commonly available but it was not the case when SWI was developed only a few years ago. Half Fourier acquisition techniques reduce scan time at most by 2 if implemented in multi-dimensions [48]. A half Fourier acquires a portion of k-space data points to reduce the acquisition time with the iterative reconstruction using a phase constrain from central k-space. The reconstructed image quality is largely dependent on how close the estimated phase is to the true phase. Ringing artifact is commonly seen with half Fourier acquisition. The advantage of half Fourier acquisition is that it's sequence independent. Single shot fast spin echo (FSE) or turbo spin echo (TSE) sequences are high speed sequences with a fast acquisition time. Single shot FSE can be combined with half Fourier acquisition technique to cut down the acquisition time even more to reach 1 second per slice, which is an excellent choice for using breath-hold to reduce motion effects in abdominal or lung imaging. However, contrast for the FSE sequence is heavily T2 weighted, which is not suitable for T2* contrast in SWI imaging. Gradient echo Echo Planar Imaging (EPI) generates similar contrast between tissues with a susceptibility

difference, as a gradient echo sequence is used in SWI imaging. Single shot EPI offers the acquisition speed. However it suffers from the following well known limitations: long echo time, low resolution, two-dimensions, and Nyquist ghosting. Segmented EPI with echo time shift (ETS) overcomes most of the limitations of single shot EPI except there is still relatively low bandwidth in the phase encoding direction. EPI is generally sampled along a Cartesian grid and reconstruction is performed using a 2D Fourier transform. Another fast imaging technique is fast spiral imaging [20], [23]. Uniform density spiral trajectory is sampled along a constant-angular-velocity spiral. In spiral imaging, off-resonance results in image blurring [23]. Interleaved fast spiral can reduce the off-resonance effect.

For the SWI sequence with a resolution of $0.5 \times 1.0 \times 2.0 \text{ mm}^3$, it takes about 16 minutes to cover the whole brain at 1.5T. To double the resolution in phase encoding direction, which is better to view the small veins [49], the scan time needs double again. To make it feasible in a clinical environment, the scan time should be limited to under 5 minutes. So we require a technique at least 4 times faster than the SWI sequence at 1.5T to cover the whole brain without significant loss of SNR. Parallel imaging or half Fourier acquisition techniques alone don't fit our goal. Both segmented EPI and interleaved fast spiral techniques are potentially viable to speed up the SWI acquisition in terms of generating $T2^*$ contrast. EPI introduces shift artifact while spiral imaging causes image blurring

due to off-resonance effect. In addition, flow compensation has to be looked into for any type of fast imaging technique to replace or combine with the standard SWI sequence. In this thesis, a segmented EPI technique was evaluated as an alternative to speed up the SWI acquisition partly because on the Siemens platform spiral imaging hasn't been used as a routine product.

Segmented Echo Planar Imaging

Partially deoxygenated venous blood is one of the examples that show unique susceptibility differences compared to the background tissues [9]. In the brain, other examples include clot (paramagnetic), calcium (diamagnetic), haemosiderin and ferritin (super paramagnetic)[40], iron-laden tissue, and of course air/tissue interfaces. In general, a sufficiently long echo gradient echo sequence (both GRE or EPI) could be used to generate a susceptibility weighted (or $T2^*$ -weighted) image to create susceptibility contrast between those tissues. 3D high-resolution Segmented Echo Planar Imaging has also been applied to study gel dosimetry where droplets produce spherical field inhomogeneity [18]. Single shot EPI suffers the following well known limitations: long echo time, low resolution, two-dimensional, equivalent low bandwidth in phase encoding direction (which results in large distortion in the PE direction), and Nyquist ghosting. Segmented EPI with echo time shift (ETS) overcomes most of the limitations except the relatively low bandwidth in the phase encoding direction. A fly-back gradient structure in the readout direction essentially eliminates the ghosting [1].

SEPI could provide an ideal alternative to speed up acquisition for susceptibility-weighted magnitude images. However, there are a few issues related to using SEPI for SWI imaging. In SEPI, phase information comes from different echo times so that it's more complicated to predict the cancellation effect. In addition to the geometric distortion, at long echo times SEPI makes both arterial and venous signal dark since all k-space is not 3D velocity compensated. This problem can be alleviated by rearranged k-space trajectory from bottom-up to center-out (making arterial signal bright). However, the center-out k-space trajectory combined with the ETS technique doubles the distortion in the phase encoding direction. Without the ETS technique, even with a fly-back gradient structure, ghosting is common for the vessels. In this thesis, we develop a new technique which utilizes the center-out k-space trajectory so that the arterial signal is bright. Instead of the ETS technique to smooth the discontinuities between the segments in k-space, an iterative phase correction technique is implemented to eliminate the discontinuities. We call the method Geometric Distortion Corrected Segmented EPI (GDC-SEPI). In front of the normal SEPI readout echo train, one additional echo is added but without any phase encoding between the added echo and the first echo on the original EPI readout to form the GDC-SEPI sequence. The idea is that now the first two echoes on the GDC-SEPI sequence sample the same central k-space. When the phase variation is relatively smooth across the whole image, we can use the sampled central k-space to estimate the phase

difference between two echoes. The phase difference then is added to later echoes iteratively so that each correction step eliminates discontinuity from one echo to the next. With the correction, each segment appears to be collected at the same echo time. The limitation of the method is investigated as well. One limitation is that the central k-space sampled should be large enough to obtain a sufficient phase estimate. The other is that the method doesn't correct the $T2^*$ effect. This can lead to a ringing artifact when the echo spacing is large or the $T2^*$ difference is large between tissues.

1.2 Overview of the thesis

1.2.1 Thesis Outline

In this thesis, we address a number of critical technical issues related to Susceptibility Weighted Imaging. We simulate CNR versus the number of phase mask multiplications in terms of constant imaging time and imaging efficiency to guide the imaging parameters associated with the acquisition of Susceptibility Weighted Imaging. We look into the partial volume effect by simulating a long cylindrical-like vessel perpendicular to the main field. With better understanding of the apparent phase behavior as a function of echo time, resolution, and imaging orientation, we could optimize the imaging protocol with the size of vessel in focus. We also develop a new image reconstruction technique for SEPI to reduce the distortion in the phase encoding direction and make both arterial and venous signal bright. Chapter 1 gives the overview of Susceptibility Weighted Imaging and problems related to the acquisition of SWI in both acquisition protocol and acquisition speed. The main body of the thesis consists of Chapter 2 through Chapter 4. Each chapter of these chapters addresses one of the issues raised in Chapter 1. At the end, Chapter 5 summarizes conclusions and points out future directions.

In Chapter 2, we look into how to enhance the CNR of the magnitude image with the multiplication of the phase mask created from the phase image.

Leaving out the partial volume effect and $T2^*$ contrast, we look at how CNR is generated alone by multiplication of a phase mask into the magnitude image. First we look at the case with a fixed SNR to see how CNR varies with the number of the phase mask multiplications for a number of phase differences between two types of tissues. This allows us to estimate the optimal number of phase mask multiplications for different phase values. We also look at how $CNR/\sqrt{\text{time}}$ changes as a function of numbers of phase mask multiplications rather than CNR itself, i.e., look at the problem from an imaging efficiency point of view.

Simulation shows that a shorter echo time has the advantage of achieving higher $CNR/\sqrt{\text{time}}$ compared with longer echo times. In terms of imaging efficiency, shorter echo time makes it possible to cover a larger volume, which is desired in a clinical environment. However, partial volume effects has to be taken into account before the optimal phase difference between venous blood and brain parenchyma can be translated to an optimal echo time.

In Chapter 3, we look into the partial volume effect of a voxel containing both venous blood and brain parenchyma. The apparent phase of a voxel depends on the vessel orientation relative to the B_0 field. We again model the vein as an infinitely long cylinder perpendicular to the main magnetic field. The results show how the apparent phase of a voxel in the image changes as a function of resolution, vessel size and, to a lesser degree, vessel center within the voxel. The simulations explain why a negative-phase mask has worked in SWI processing of

high-resolution images collected in the transverse direction, despite the expected positive-phase behavior for vessels perpendicular to the main field.

In Chapter 4, we develop a Geometric Distortion Corrected Segmented EPI sequence to speed up moderately the SWI acquisition while reducing the distortion of SEPI and overcoming the problem of both dark arterial and venous signal. GDC-SEPI utilizes the center-out k-space trajectory so that the arterial signal is bright. Instead of the ETS technique to smooth the discontinuities between the segments in k-space, an iterative phase correction technique is implemented to eliminate the discontinuities. With the correction, each segment appears to be collected at the same echo time. The limitation of the method is investigated as well.

1.2.2 Contributions and Related Publications

The Author has contributed to the following original work included in this thesis:

1. In Chapter 2, a method to optimize the contrast to noise ratio (CNR) of SWI image as a function of the number of multiplications of the phase mask created from the phase image.
2. In Chapter 3, a method to estimate partial volume effect of apparent voxel phase vs. the resolution, and image orientation.
3. In Chapter 4, a new image reconstruction technique for Segmented EPI to speed the SWI acquisition.

In addition to the contributions listed above, the author made a significant effort to make the sequences work on the Siemens Syngo platform for acquisition of SWI data presented in all Chapters. The contents of Chapter 2 have been published in MRM [9]. The contents of Chapter 3 have been published in MRI [49]. The contents of Chapter 4 have been submitted to MRI and now after a revision process they have been remitted.

Chapter 2

Optimization of Post Processing

(Chapter 2 is an article published in Journal of Magnetic Resonance in Medicine.

Haacke EM, Xu Y, Cheng YN, Reichenbach JR, Susceptibility Weighted Imaging (SWI), *MRM*, 2004, 52:612-618.)

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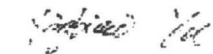
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Susceptibility Weighted Imaging (SWI)

E. Mark Haacke,^{1-4*} Yingbiao Xu,^{1,2} Yu-Chung N. Cheng,¹ and Jurgen R.

Reichenbach⁵

¹Dept. of Radiology, Wayne State University, Detroit, Michigan.

²MRI Institute for Biomedical Research, Detroit, Michigan.

³Dept. of Physics, Case Western Reserve University, Cleveland, Ohio.

⁴Dept. of Radiology, Loma Linda University, Loma Linda, California.

⁵Institute of Diagnostic and Interventional Radiology, Friedrich Schiller University,
Jena, Germany.

*Correspondence to: E. Mark Haacke, 440 E. Ferry Street, Unit 2, Detroit, MI 48202. E-mail: nmrimaging@aol.com, rdmlaze@yahoo.com

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Susceptibility differences between tissues can be utilized as a new type of contrast in MRI that is different from spin density, $T1$ -, or $T2$ -weighted imaging. Signals from substances with different magnetic susceptibilities compared to their neighboring tissue will become out of phase with these tissues at sufficiently long echo times (TEs). Thus, phase imaging offers a means of enhancing contrast in MRI. Specifically, the phase images themselves can provide excellent contrast between gray matter (GM) and white matter (WM), iron-laden tissues, venous blood vessels, and other tissues with susceptibilities that are different from the

background tissue. Also, for the first time, projection phase images are shown to demonstrate tissue (vessel) continuity. In this work, the best approach for combining magnitude and phase images is discussed. The phase images are high-pass-filtered and then transformed to a special phase mask that varies in amplitude between zero and unity. This mask is multiplied a few times into the original magnitude image to create enhanced contrast between tissues with different susceptibilities. For this reason, this method is referred to as susceptibility-weighted imaging (SWI). Mathematical arguments are presented to determine the number of phase mask multiplications that should take place. Examples are given for enhancing GM/WM contrast and water/fat contrast, identifying brain iron, and visualizing veins in the brain.

Key words: magnetic susceptibility; phase imaging; water/fat separation; artery/vein separation; imaging iron

A number of important tissues have unique magnetic susceptibility differences relative to background or surrounding tissues. One such example is partially deoxygenated venous blood (1–3). Other examples include clot (paramagnetic), calcium (diamagnetic) (4), and iron-laden tissue (5), and air/tissue interfaces. These bulk magnetic susceptibilities are indistinguishable from chemical shift effects. The most common example of the latter in magnetic resonance imaging (MRI) is the chemical shift difference between water and fat. Usually chemical shift effects are ignored, but in the case of water and fat separation (6–8) the 3.35-ppm difference is used to separate water and fat. On the other hand, if information regarding several species occupying the same voxel is desired, one usually obtains the spectral information by collecting a time series of data and Fourier transforming the data. This is referred to as chemical shift imaging.

However, when only a single element or tissue component is present in a voxel, or if there is a dominant element in each voxel, it is possible in some circumstances to extract spectral information from the phase alone. The phase image itself can then be used to separate the dominant spectral information on a pixel-by-pixel basis. This concept has been used in a single point water/fat separation approach (7) and in imaging velocity using phase in MR angiography (MRA) (9). The problem with phase images has generally been the presence of background local fields that confound the effects of local phase changes in tissue. However, when the phase changes between tissues have a high spatial frequency,

these unwanted global effects essentially can be removed (8). Once this is accomplished, the door is open for new applications of phase imaging to highlight or differentiate one type of tissue from another. First, the phase itself can be a superb source of image contrast. This has already been demonstrated for GM/WM contrast (10), small veins in the brain (11), and more recently in venous blood vessels in the peripheral vasculature (8). Second, the phase can be used as a mask to create magnitude images with suppressed/enhanced spectral components or modified contrast. Third, the phase images themselves can be used to create projection images to show tissue (vessel) contiguity. Here we consider single time point methods to enhance the contrast of certain tissues containing fat, venous blood, or iron. Since we focus on the role of susceptibility, and use the original phase image both by itself and as a means of altering the contrast in the magnitude images, we refer to this method as susceptibility weighted imaging (SWI) (12). Although SWI has been used as an MR venographic method for several years (13–26), it has more recently been applied to studies of arterial venous malformations (16,24), occult venous disease (15), multiple sclerosis (20), trauma (25), tumors (21,23,26), and functional brain imaging (14,22). Given the continued increasing clinical interest in this topic, it is important to ensure a complete understanding of the mathematical processes involved in creating SW images.

MATERIALS AND METHODS

Our goal in this work was to use phase to enhance contrast between tissues with different susceptibilities. This can be accomplished in several steps. First, we employ the high-pass filter described in Ref. 8 to remove the low-spatial frequency components of the background field. In the work shown here, we use a 64 x 64 low-pass filter and divide this into the original phase image (512 x 512) to create a high-pass filter effect.

Second, this “corrected” phase image is used to create a “phase” mask that is used to multiply the original magnitude image to create novel contrasts in the magnitude image. The phase mask is designed to suppress those pixels that have certain phases. It is usually applied in the following manner: If the minimum phase of interest is, for example, $-\pi$, then the phase mask is designed to be $f(x) = (\phi(x) + \pi)/\pi$ for phases < 0 , and to be unity otherwise, where $\phi(x)$ is the phase at location x . That is, those pixels with a phase of $-\pi$ will be completely suppressed and those with a value between $-\pi$ and zero phase will be only partly suppressed. This phase mask ($f(x)$) then takes on values that lie between zero and unity. We will refer to it as the negative phase mask. It can be applied any number of times (integer m) to the original magnitude image ($\rho(x)$) to create a new image $f^m(x)$ $\rho(x)$ with different contrasts (11,13,22). Another mask might be defined to highlight positive phase differences:

$$\rho(x)_{\text{new}} = g^m(x) \rho(x) \quad [1]$$

If the maximum phase of interest is, for example, π , then the phase mask is designed to be $g(x) = (\pi - \phi(x))/\pi$ for phase > 0 , and unity otherwise. We will refer to this as the positive phase mask. Alternatively, if echo times (TEs) are so long that they cause difficulties, or if it is desirable to calculate phase from very short TEs without any RF penetration phase effects, an interleaved double-echo scan can (29) be acquired to simulate the equivalent phase of a short-TE scan. The complex data from the first echo are then divided into those of the second echo to create an equivalent phase image to that for a TE of ΔTE . That is, the phase in the complex division becomes $-\gamma \Delta B \Delta TE$. We use this concept to create an effective TE = 2 ms image from an interleaved TE = 8 ms and TE = 10 ms data set. All sequences used in this study were high-resolution, 3D gradient-echo scans. In-plane resolution varied from 0.5 mm x 0.5 mm to 1 mm x 1 mm with slice thicknesses of 0.7–2 mm. Except for the interleaved double-echo experiment for highlighting fat described above, the experiments were run with TE = 40 ms. These experiments were all performed at 1.5T except for one case in which the data were obtained at 3.0T.

Phase Mask Multiplication: Theoretical Considerations

Phase masks are created to enhance the contrast in the original magnitude images. Depending on the constructs used to create the filter, the number of multiplications needed to optimize the contrast-to-noise ratio (CNR) in the SW images will vary. We consider the positive phase mask case below. The results for

the negative phase mask follow by letting ϕ go to $-\phi$. The first step is to write an expression for the CNR between two tissue types. Consider first the example in which all tissues have the same signal S_0 with Gaussian noise, and contrast is generated only by the phase images. The contrast in the magnitude image is therefore zero. Contrast appears only after multiplication by the phase mask has been performed. We create a function that is dependent on m , the number of multiplications that are performed with the phase mask. The goal is to optimize m or, equivalently, find the point at which $\text{CNR}(m)$ is maximized. The region of the object where there is a phase difference will then change its signal after multiplication with the phase mask. For the positive phase mask considered here, the multiplication factor of the signal will become $(1-\phi/\pi)^m$ in the positive-phase region, while that in the negative-phase region remains unity. The inherent contrast that develops will then be $1-(1-\phi/\pi)^m$ times S_0 of the object in the original magnitude image. The noise in the new image must take into account the noise in the original image plus the noise generated from the multiplications. For a high signal-to-noise ratio (SNR) in the magnitude images ($>4:1$), the variance of the final image after m multiplications is given by

$$\sigma_i^2 = \sigma_0^2 (1 + (m/(2\pi))^2 + (1 - \phi/\pi)^{2m} + (m/\pi)^2 (1 - \phi/\pi)^{2m-2}) \quad [2]$$

where σ_0 is the standard deviation (SD) of the Gaussian noise in the original magnitude image (see the Appendix for a full derivation). Therefore, the functional form for $\text{CNR}(m)$ is the contrast divided by the noise, and is given by

$$CNR(m) = SNR_0 (1 - (1 - \varphi / \pi)^m) / \sqrt{1 + (m/(2\pi))^2 + (1 - \varphi / \pi)^{2m} + (m/\pi)^2 (1 - \varphi / \pi)^{2m-2}} \quad [3]$$

where SNR_0 is the original SNR (i.e., S_0 / σ_0). When the exponential decay of the MR signal is included in our analysis, the $CNR(m)$ becomes:

$$SNR_0 \exp(-\varphi / \pi) (1 - (1 - \varphi / \pi)^m) / \sqrt{1 + (m/(2\pi))^2 + (1 - \varphi / \pi)^{2m} + (m/\pi)^2 (1 - \varphi / \pi)^{2m-2}} \quad [4]$$

where we have assumed that $TE/T2^*$ is unity when $\varphi = \pi$ (since it is just the increase in signal for shorter TE and hence smaller m that we are after here). The more general form can be obtained by replacing $\exp(-\varphi/\pi)$ with $\exp((- \varphi/\pi)T2^*/TE)$. However, $T2^*$ plays a role in the signal decay, and we can not arbitrarily choose a long TE to get the phase to be π without a great loss in SNR. Thus, when the phase is π , there will be circumstances in which the number of multiplications required will be >1 in order to show the optimal contrast in the images. This raises an interesting question. If one is willing to spend a fixed amount of time imaging (specifically, to acquire a long enough TE to ensure that the phase is π), then it is not clear whether a shorter TE with more phase multiplications might not do just as good a job. That is, it might be better to look into reducing the TE (and hence the TR), collecting the data with a shorter TE (i.e., with a higher signal), performing more multiplications, and averaging over several acquisitions in order to obtain an optimal CNR.

For the case of the same volume coverage as well as the same imaging time, one then considers the efficiency $\text{CNR} \cdot \sqrt{\text{number of slices}} / \sqrt{\text{time}}$ rather than the CNR. This introduces another factor of $\sqrt{\pi/\varphi}$ into the right-hand side of Eq. [4] such that CNR is proportional to (although we ignore the need to increase the read gradient strength when TR becomes too short):

$$\frac{\text{SNR}_0 \sqrt{\pi/\varphi} \exp(-\varphi/\pi) (1 - (1 - \varphi/\pi)^m)}{\sqrt{1 + (m/(2\pi))^2 + (1 - \varphi/\pi)^{2m} + (m/\pi)^2 (1 - \varphi/\pi)^{2m-2}}} \quad [5]$$

This term arises because the only way to collect these data is to either increase the overall time by acquiring the data a second time or use a segmented echo-planar-like approach, which in turn requires that the gradient strength be increased accordingly. When the gradient strength is increased (such that both the sampling time and TE are decreased), then a factor of $\sqrt{\varphi}$ loss in SNR occurs, and Eq. [5] reduces once again to Eq. [4]. If one is interested in comparing images with circular objects of radius p pixels, (Fig. 1) then one can look at visibility v instead of CNR (29), where

$$v = \text{CNR}(m) \cdot p \sqrt{\pi} \quad [6]$$

In the plots for Figs. 2 and 3, we have taken $p = 2$.

Phase Mask Multiplication: Simulations

We created a series of circles by simulating a Fourier transform experiment with a 512×512 acquisition matrix (i.e., pixels). The radius of the circles varies from one to 16 pixels (see Fig. 1). Within each circle, the phase value is set to be 0.3π .

The initial signal intensity of all pixels within the image is set to be 1500. A Gaussian noise with an SD of 100 is added to each real and imaginary channel. Finally, a magnitude image and a phase image are reconstructed from the real and imaginary channels. The SNR of the magnitude image is then 15:1. A region of interest (ROI) is drawn inside and outside of each circle to obtain the CNR between the two ROIs.

RESULTS

Number of Multiplications

The predictions of Eq. [3] are shown in Fig. 2a. They validate previous work in this area (11,13), and indicate that three to five multiplications provide the best contrast when the veins are enhanced. The veins vary in their phase behavior, with those perpendicular to the main field having a phase of at most $-\pi/2$. In that case, $\text{CNR}(m)$ is predicted to peak for $m = 4$. However, many vessels will be partial-volumed (even those parallel to the main field) so that there will be a spread of phases. The lower the phase, the larger the m necessary to obtain the optimal contrast; however, an m of 3–5 is shown to create good contrast for many different values of ϕ . To test the theory more extensively, we compare next the measured values of $\text{CNR}(m)$ for the simulated data described above. We plot the results in Fig. 2b. The results are in good agreement, given the approximations made about large SNR. The simulated images in Fig. 1 demonstrate that the best CNR is obtained with an m of about 4, but even an m of 8 gives a good CNR. The image with an m of 16 is clearly as noisy as the image with m equal to one. From

a practical point of view, given that noise is increased as m increases, the best value of m to choose is the smallest one that meets the desired CNR. This is particularly true if a minimum intensity projection (mIP) is to be performed afterward, because the more noise that is present, the worse the mIP will be. As discussed above, there will be times when it may be more expedient to collect the data at shorter TE but in a given fixed total time period. The results of these predictions are shown in Fig. 3. The curves suggest that choosing a TE such that the phase is 0.3π (Eq. [5]) to 0.5π (Eq. [4]) may be the best way to collect the data for optimal SNR and spatial coverage.

Filtered Phase Imaging

This example focuses on visualizing water and fat in a single image. Here we use the data acquired from a double gradient-echo scan with TEs of 8 and 10 ms. The magnitude image from the TE = 8 ms image is shown in Fig. 4a. By complex-dividing the TE = 8 ms image into the TE = 10 ms image, we create a phase image with $\Delta TE = 2$ ms (Fig. 4b). Such a short TE avoids the problems associated with aliasing caused by the inhomogeneities near the air/tissue interfaces in the sinuses near the orbit for the original longer-TE scans. This value of 2 ms was chosen to obtain fat roughly π out of phase with water (although this condition is not necessary in order for the method to work). The resulting phase images are essentially alias-free and well smoothed compared to the original data. The phase itself clearly discriminates water and fat without the need for any anti-aliasing

programs or fat saturation. The optic nerve is well shown, buried in the surrounding muscle.

Enhancing Magnitude Contrast

Continuing with the water/fat example, when the negative phase mask is used once, the fat is nicely suppressed (Fig. 4c); however, when it is used twice, the fat is dramatically reduced in amplitude but is not eliminated (Fig. 4d). The former image gives excellent contrast in the $T1$ -weighted image, which still includes some fat signal (this is still of value when the images are clinically reviewed). A separate fat image can be obtained by subtracting this image from the original unprocessed image, or by just using the phase image itself as a means of visualizing the water and fat separately.

A second application of the phase images is the enhancement of GM/WM contrast in $T1$ -weighted imaging. We ran a $T1$ -weighted scan with $TE = 5$ ms, and then followed this with an SWI scan with $TE = 40$ ms on a 1.5T system. Both scans have the same resolution (0.5 mm x 1 mm x 2 mm) and cover the same ROI. Figure 5a shows the 5-ms data. We used the phase image of the same slice position from the 40-ms data set of the SW scan to create a phase mask. Then we multiplied the phase mask into the magnitude image (Fig. 5a) four times to create a phase-masked image (Fig. 5b), which showed an enhanced contrast and better edge definition as well (although, as expected, the image was a little noisier). As a

third example of phase-enhanced magnitude contrast, we revisit the application to the venous blood vessels in the brain. Given that the susceptibility difference between fully oxygenated and deoxygenated blood is 0.18 ppm in cgs units, as reported in Ref. 28, a rather long TE of 40 ms is required to visualize large phase differences. Vessels parallel to the field will show a negative phase inside the vessels, and those perpendicular to the field will show a positive phase inside the vessels (29). However, due to finite voxel size (and hence partial volume effects), as well as aliasing of the external fields outside the vessels, the perpendicular vessels may appear to have a negative phase when the resolution is low. In Fig. 6, we show an example from a 3T system with a resolution of 0.5 mm x 0.5mm x 1.0 mm. The data set was collected in a transverse orientation, with the z-direction (the main field direction) being slice-select (i.e., the slices are 1 mm thick). To demonstrate the value of the phase mask, we show in Fig. 6a and 6b an mIP over 12 slices without and with, respectively, the special phase processing. Actually, the phase images themselves can be mIPped (Fig. 6c), and they reveal why this method works so well: all of the vessels that are enhanced over and above the cancellation already present in the magnitude images are shown in this mIP. This is the first time that phase images have been used to generate a projection that in and of itself has potential value.

DISCUSSION AND CONCLUSIONS

Phase images contain direct information about the background magnetic field and chemical shift of tissues. The ability to use the phase for spectroscopic information depends, in part, on the elimination of phase from the background field, and partial volume effects with other tissues that have different chemical shifts. When it comes to the ideal choice of mask multiplication, partial volume effects can modify the simple arguments of a one-compartment model. In these cases, a series of multiplications may be best—or at least that image that can simultaneously enhance the contrast for all cases would be the best image to display. For example, if the blood vessel is so small that a phase of 90° turns into a phase of 45° , then it will take more multiplications to bring out a better contrast. Those vessels that still show phases of 90° will not be hurt much by the use of more multiplications. This special number of multiplications usually turns out to be about 3, 4, or 5. This choice also keeps the CNR drop to a factor of less than $\sqrt{2}$. From Fig. 2, we can see there is a trade-off between the gain of CNR and loss of SNR by means of phase multiplication before CNR reaches its peak. Afterwards, CNR and SNR both decrease as the number of multiplications increases.

Number of Multiplications

Although partial volume effects are often problematic, they turn out to be rather useful in our implementation of the phase-masking process. For vessels perpendicular to the main field, we expect the phase to be positive inside the

vessel when the vessel is the size of a pixel. The partial volume effect apparently reverses this behavior for transverse images when the vessel is smaller than the in-plane voxel size, and the slice is twice as thick (or more) as the in-plane voxel size. The phase now appears to be negative but much smaller than π . As shown in Fig. 3, even with a lower phase value, we can enhance the presence of a vessel by performing a phase mask with m about 4. This is demonstrated in Fig. 6c, where the phase of the perpendicular vessels is clearly negative and varies from vessel to vessel. At longer TE, if the phase at the boundary aliases, the phase multiplication results in fatter vessels. There is a potential problem here. In more complicated cases, the phase might change sign and make the processing less effective and the interpretation of the resulting images less clear. However, in practice this has not been a problem. One way to avoid this difficulty is to use constant time imaging, which allows for a reduced TE but does not require a large phase shift. To overcome this, more multiplications must be performed (up to eight to 10 for a phase of only 0.1π ; Fig. 3b). Nevertheless, it is quite interesting that such a low phase difference can lead to an excellent increase in contrast. This may have important implications for observing areas of small changes in iron content or small blood vessels.

Water/Fat Separation

In Fig. 4, the effective TE time is 2 ms. This value was chosen so that we could obtain fat roughly π radians out of phase with water (although this is not a

necessary condition for this method to work), so that with one or two multiplications the fat signal would be effectively suppressed. With this effective short TE, we can see the strong differences between the complicated phase in the original images and the unwrapped phase image (Fig. 4b). With high resolution to reduce the partial volume effect, and high bandwidth to reduce the signal shift from fat, this means of suppressing fat becomes more viable. Nowadays, the TE can be < 2 ms for a fast gradient-echo sequence, so without having to acquire a data set twice to create the equivalent short-TE phase image (as in Fig. 4), we can use the phase image itself by filtering out the background phase effects first to do the same job. The phase image clearly discriminates between water and fat without the need for any anti-aliasing programs or fat saturation when small TEs are used. The phase from global background field inhomogeneities might still add to the phase contributed by the fat chemical shift, causing aliasing. This would prevent the method from working perfectly, but for these short TEs this is unlikely to be a problem.

Phase Filtering

At these long TEs, because of the excess aliasing, the high-pass filter cannot remove all the background phase effects from air/tissue interfaces, which then generate a false contrast that is not caused by vessels. However, since we know where these problems occur (such as near the sinuses), we can avoid interpreting the data in these areas. We have tried using a multiecho approach to remove all

background field effects except those due to partial voluming (i.e., small vessels only), with some success. More recent attempts have involved an alternative to homodyne filtering that works directly on the reconstructed phase images, as in Ref. 30. Further work in this area would be useful to remove remnant air/tissue field inhomogeneity effects. Finally, if these remnant errors can be removed, phase images and projections over phase images may play a more important role in presenting new contrast features.

Acquisition Time

Given the fact that this is a 3D, long-TR acquisition scheme, it can take 8 min to acquire the data with 32 partitions and a matrix size of 256 (phase) x 512 (read). Apart from the above-mentioned background field effects on the phase, this is perhaps the major impediment to this method. However, segmented EPI has the potential to reduce the imaging time by at least a factor of 2 and perhaps 4 (work in progress), and parallel imaging may reduce it by another factor of 2. Therefore, at 1.5T it will become possible to collect the data with 64 partitions in 2–4 min, while at 3T the TR can be cut in half (since the TE can be cut in half), making it possible to collect 128 slices (whole brain coverage) in just 2–4 min.

CONCLUSIONS

SWI continues to find applications in both research and clinical areas. A proper understanding of its processes is of paramount importance for obtaining images

with the best contrast possible. In this work we have explained how the current processing methods work, and introduced several new concepts to enhance contrast based on the use of phase images and constant time imaging.

ACKNOWLEDGMENTS

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APPENDIX

Calculation of the CNR Between two Pixels in an SW Image

In this Appendix, the CNR between two pixels in an SW image is calculated.

These two pixels are labeled as one and two. In an original magnitude image, the two pixels have signals S_1 and S_2 . The corresponding noises (SDs of the Gaussian noises) in the two pixels are σ_1 and σ_2 such that the SNRs are $\text{SNR}_1 (= S_1/\sigma_1)$ and $\text{SNR}_2 (= S_2/\sigma_2)$, respectively. The phases of these two pixels are φ_1 and φ_2 . The SDs of the corresponding pixels in the phase image are assumed to be $d\varphi_1 (\approx \sigma_1/S_1)$ and $d\varphi_2 (\approx \sigma_2/S_2)$, respectively. When SNR is close to unity, the noise distribution is no longer Gaussian. In that case, the Rayleigh distribution has to be considered such that the SD of the noise can be correctly calculated.

Suppose we consider a function, $h(\varphi, m)$, that consists of m multiplications of the positive phase mask, i.e., the value of this function is $(1 - \varphi/\pi)^m$ when φ is between 0 and π , and the value is set to be one when φ is between $-\pi$ and 0. When φ is positive, the SD of this function is

$$\sigma_h = (m / \pi)(1 - \varphi / \pi)^{m-1} d\varphi \quad [A_1]$$

When φ is negative, the SD is zero (i.e., no noise is introduced in this region).

When φ is 0, the SD is $(m/(2\pi)) d\varphi$, where the extra factor 1/2 is due to the discontinuity. These results can be derived from the concept of error propagation.

The SW image is created by the multiplication of the magnitude image and the function $h(\varphi, m)$. If the signal of a pixel in the magnitude image is S with noise (SD) σ , then the overall signal in the SW image is $h(\varphi, m)S$, and the noise is the square root of the variance, which is $h^2(\varphi, m)\sigma^2 + S^2\sigma_h^2$, where σ_h is the SD of $h(\varphi, m)$.

Thus, the CNR between two pixels is the difference of the SNRs of the two pixels, which is $|S_1h_1 - S_2h_2|/\sigma_t$, where σ_t is the square root of

$$h_1^2\sigma_1^2 + h_2^2\sigma_2^2 + S_1^2(\sigma_{h1})^2 + S_2^2(\sigma_{h2})^2 \quad [A_2]$$

In our simulated images, the signals in the magnitude images are uniform, i.e., $S \equiv S_1 = S_2$. The SDs of noise levels of all pixels in the magnitude images are also identical, i.e., $\sigma \equiv \sigma_1 = \sigma_2$. The phase outside the black disks is zero, i.e., $h_1(0, m) = 1$ and $S_1(\sigma_{h1}) = (m/(2\pi))\sigma$. Thus, the CNR between two sets of pixels is

$$CNR = SNR(1 - (1 - \varphi/\pi)^m) / \sqrt{1 + (m/(2\pi))^2 + (1 - \varphi/\pi)^{2m} + (m/\pi)^2(1 - \varphi/\pi)^{2m-2}} \quad [A_3]$$

where $SNR \equiv S/\sigma$. This analysis applies to the negative phase mask when φ is replaced by $-\varphi$.

REFERENCES

1. Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci USA* 1990;87:9868–9872.
2. Ogawa S, Lee TM. Magnetic resonance imaging of blood vessels at high fields: in vivo and in vitro measurements and image simulation. *Magn Reson Med* 1990;16:9–18.
3. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magn Reson Med* 1990;14:68–78.
4. Yamada N, Imakita S, Sakuma T, Takamiya M. Intracranial calcification on gradient-echo phase image: depiction of diamagnetic susceptibility. *Radiology* 1996;198:171–178.
5. Ogg RJ, Langston JW, Haacke EM, Steen RG, Taylor JS. The correlation between phase shifts in gradient-echo MR images and regional brain iron concentration. *Magn Reson Imaging* 1999;17:1141–1148.
6. Dixon WT. Simple proton spectroscopic imaging. *Radiology* 1984;153:189–194.
7. Haacke, EM, Patrick JL, Lenz GW, Parrish T. The separation of water and lipid components in the presence of field inhomogeneities. *Rev Magn Reson Med* 1986;1:123–154.

8. Wang Y, Yu Y, Li D, Bae KT, Brown JJ, Lin W, Haacke EM. Artery and vein separation using susceptibility-dependent phase in contrast-enhanced MRA. *J Magn Reson Imaging* 2000;12:661–670.
9. Bryant DJ, Payne JA, Firmin DN, Longmore DB. Measurement of flow with NMR imaging using a gradient pulse and phase difference technique. *J Comput Assist Tomogr* 1984;8:588–593.
10. Haacke EM, Lai S, Yablonskiy DA, Lin W. In vivo validation of the BOLD mechanism: a review of signal changes in gradient echo functional MRI in the presence of flow. *Int J Imaging Syst Technol* 1995;6:153–163.
11. Reichenbach JR, Venkatesan R, Schillinger DJ, Kido DK, Haacke EM. Small vessels in the human brain: MR venography with deoxyhemoglobin as an intrinsic contrast agent. *Radiology* 1997;204:272–277.
12. U.S. patent no. 6501272 B1, issued 31 December 2002; and U.S. patent no. 6658280, issued 2 December 2003.
13. Reichenbach JR, Essig M, Haacke EM, Lee BC, Przetak C, Kaiser WA, Schad LR. High resolution venography of the brain using magnetic resonance imaging. *MAGMA* 1998;6:62–69.
14. Baudendistel KT, Reichenbach JR, Metzner R, Schroöder J, Schad LR. Comparison of functional venography and EPI-BOLD-fMRI at 1.5T. *Magn Reson Imaging* 1998;16:989–991.
15. Lee BCP, Vo KD, Kido DK, Mukherjee P, Reichenbach J, Lin W, Yoon MS, Haacke EM. MR high-resolution blood oxygenation level-dependent

- venography of occult (low-flow) vascular lesions. *AJNR Am J Neuroradiol* 1999;20:1239–1242.
16. Essig M, Reichenbach JR, Schad LR, Schoenberg SO, Debus J, Kaiser WA. High-resolution MR venography of cerebral arteriovenous malformations. *Magn Reson Imaging* 1999;17:1417–1425.
17. Lai S, Glover GH, Haacke EM. Spatial selectivity of BOLD contrast: effects in and around draining veins. In: Moonen CRW, Bandettini PA, editors. *Medical radiology. Diagnostic imaging and radiation oncology*. Berlin: Springer-Verlag; 1999.
18. Lin W, Mukherjee P, An H, Yu Y, Wang Y, Vo K, Lee B, Kido D, Haacke EM. Improving high-resolution MR BOLD venographic imaging using a T1 reducing contrast agent. *J Magn Reson Imaging* 1999;10:118–123.
19. Reichenbach JR, Barth M, Haacke EM, Klarhofer M, Kaiser WA, Moser E. High-resolution MR venography at 3 Tesla. *J Comput Assist Tomogr* 2000;24:949–957.
20. Tan IL, van Schijndel RA, Pouwels PJW, van Walderveen MAA, Reichenbach JR, Manoliu RA, Barkhof F. MR venography of multiple sclerosis. *AJNR Am J Neuroradiol* 2000;21:1039–1042.
21. Reichenbach JR, Jonetz-Mentzel L, Fitzek C, Haacke EM, Kido DK, Lee BCP, Kaiser WA. High-resolution blood oxygen-level dependent MR venography (HRBV): a new technique. *Neuroradiology* 2001;43:364–369.

22. Reichenbach JR, Haacke EM. High-resolution BOLD venographic imaging: a window into brain function. *NMR Biomed* 2001;14:453–467.
23. Schad L. Improved target volume characterization in stereotactic treatment planning of brain lesions by using high-resolution BOLD MRvenography. *NMR Biomed* 2001;14:478–483.
24. Essig MM, Reichenbach JR, Schad LL, Debus JJ, Kaiser WA. High resolution MR-venography of cerebral arteriovenous malformations. *Radiologe* 2001;41:288–295.
25. Tong KA, Ashwal S, Holshouser BA, Shutter L, Herigault G, Haacke EM, Kido DK. Improved detection of hemorrhagic shearing lesions in children with post-traumatic diffuse axonal injury—initial results. *Radiology* 2003;227:332–339.
26. Barth M, Nobauer-Huhmann IM, Reichenbach JR, Mlynarik V, Schoggel A, Matula C, Trattnig S. High-resolution three-dimensional contrastenhanced blood oxygenation of brain tumors at 3 Tesla: first clinical experience and comparison with 1.5 Tesla. *Invest Radiol* 2003;38:409–414.
27. Abduljalil AM, Schmalbrock P, Novak V, Chakeres DW. Enhanced gray and white matter contrast of phase susceptibility-weighted images in ultra-high-field magnetic resonance imaging. *J Magn Reson Imaging* 2003;18:284–290.

28. Weiskoff RM, Kiihne S. MRI susceptometry: image-based measurement of absolute susceptibility of MR contrast agents and human blood. *Magn Reson Med* 1992;24:375.
29. Haacke EM, Brown RW, Thompson MR, Venkatesan R. *Magnetic resonance imaging, physical principals and sequence design*. New York: Wiley-Liss; 1999. p 741–771.
30. Rauscher A, Barth M, Reichenbach JR, Stollberger R, Moser E. Automated unwrapping of MR phase images applied to BOLD MR-venography at 3 Tesla. *J Magn Reson Imaging* 2003;18:175–180.

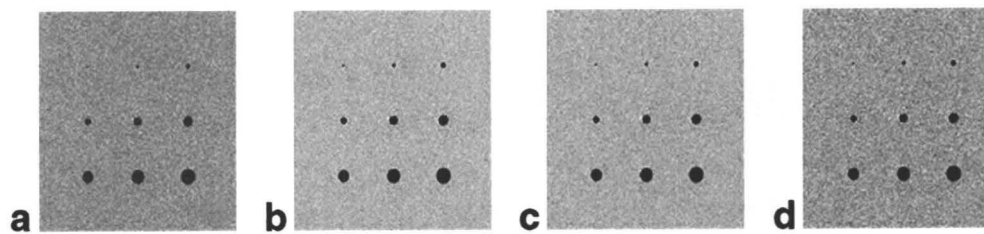


FIG. 1. Simulated images with the phase mask multiplied (a) once, (b) four times, (c) eight times, and (d) 16 times. The radius of the circles varied from one to 16 pixels. All circles have the same phase value of 0.3π . The SNR of the original magnitude image was 15:1.

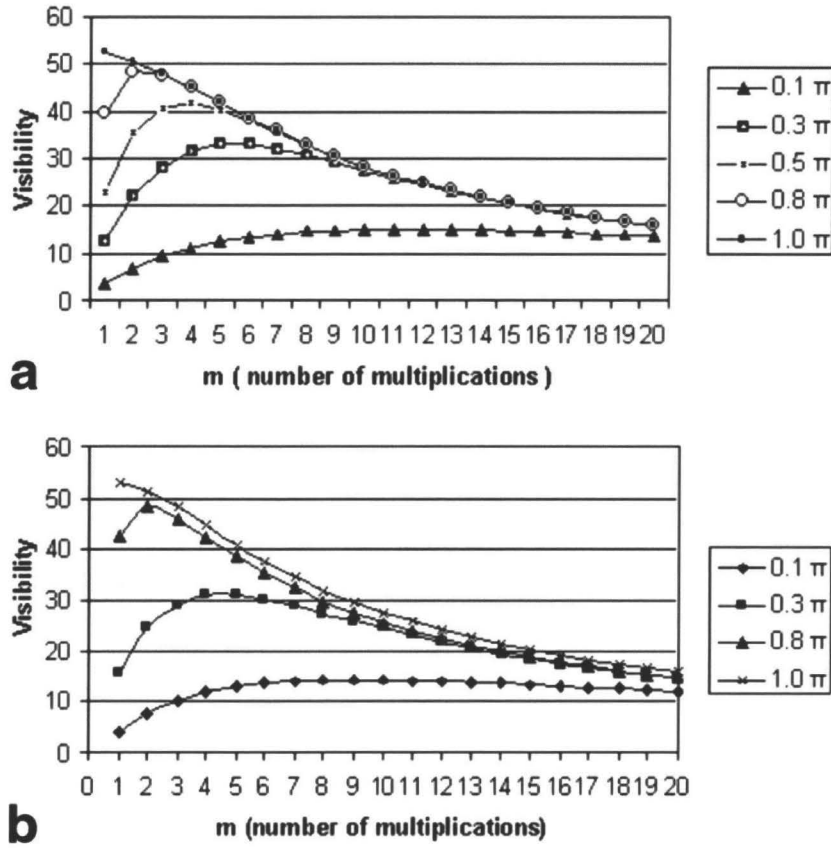


FIG. 2. a: Visibility as a function of multiplication ($2\sqrt{\pi} \times \text{Eq. [3]}$). Note that the smaller the phase value, the larger the multiplication required to reach the maximum CNR. b: Visibility as measured in the simulated images in Fig. 1 as a function of multiplication. Note that the results are in good agreement with the theoretical predictions shown in a.

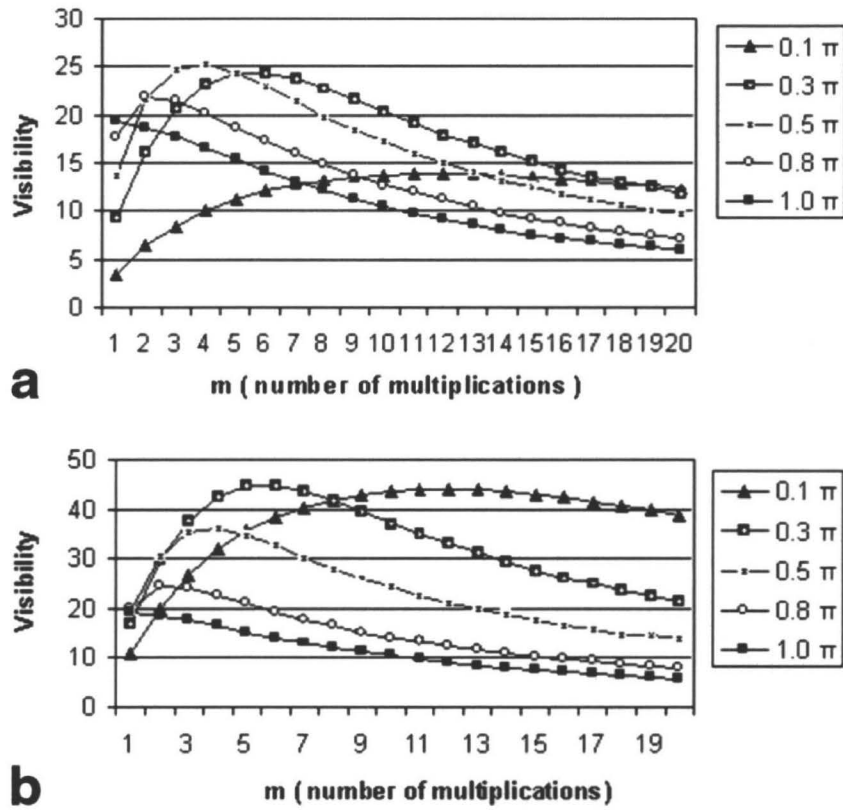


FIG. 3. Plots of visibility show the predictions of (a) $v/\sqrt{\text{time}}$ and (b) $v/\sqrt{\text{number of slices}}/\sqrt{\text{time}}$ as a function of the number of multiplication ($2\sqrt{\pi} \times \text{Eq. [4]}$ and $2\sqrt{\pi} \times \text{Eq. [5]}$). The curves suggest that choosing a TE such that the phase is (a) 0.5π or (b) 0.3π may be the best way to collect the data for optimal SNR and optimal coverage, respectively.

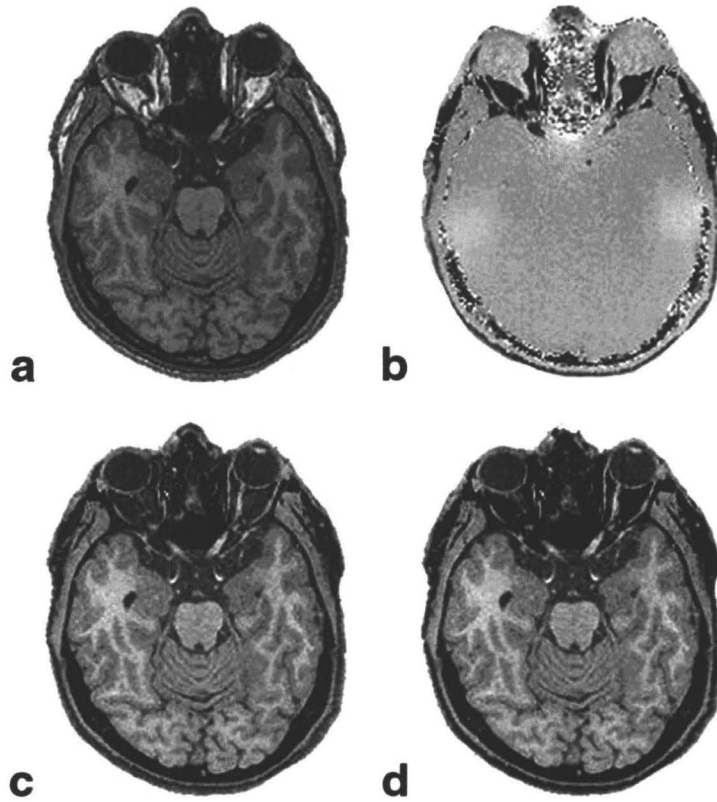


FIG. 4. A demonstration of the visualization of fat and water with phase information. **a**: The original magnitude image with TE = 8 ms. **b**: The equivalent TE of the 2 ms phase image resulting from the complex division of TE = 10 ms and 8 ms images. **c** and **d**: SW images of part **a** after the phase mask (**b**) was multiplied one and two times, respectively. Note that the fat signal is effectively suppressed around the optic nerve in **c** and **d**.

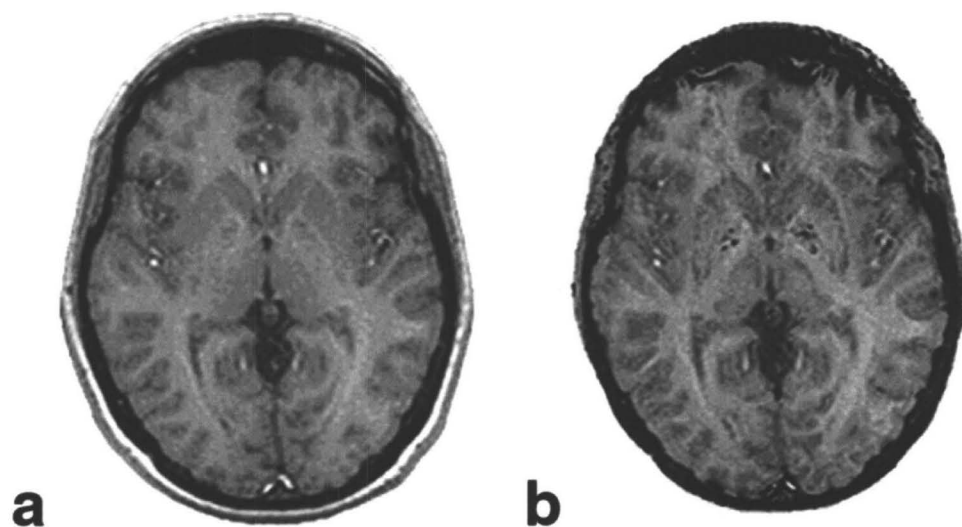


FIG. 5. A demonstration of the utilization of the phase image from SWI to enhance GM/WM contrast in T_1 -weighted imaging. **a:** T_1 -weighted magnitude image of $TE = 5$ ms. **b:** The same magnitude image as in part **a**, with $m = 4$ using the phase mask from the $TE = 40$ ms data. Note the enhanced contrast between GM and WM in the lower half of the image. Some mineralization in the globus pallidus is also revealed. Some artifacts are introduced at the top of the image because of the local field inhomogeneity caused by the sinus.

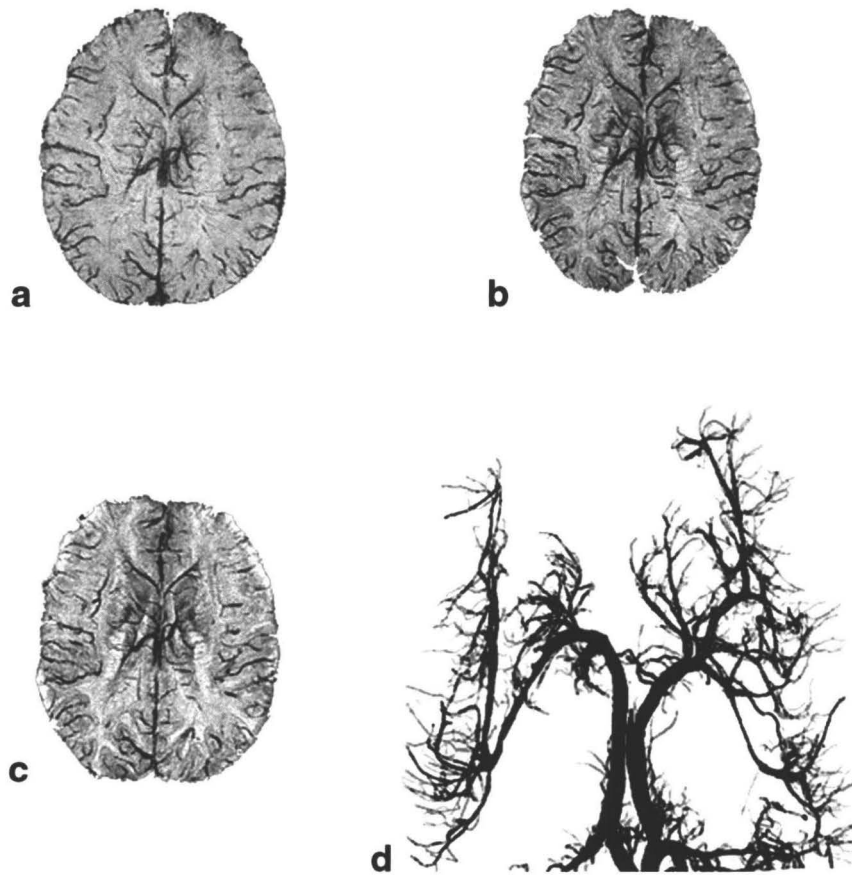


FIG. 6. **a:** mIP of the original magnitude images without any phase mask multiplication. **b:** Modified mIP of SW images using $m = 4$. **c:** mIP of filtered phase images. **d:** A slice from a cadaver brain, which can be compared to the middle section of the images shown in **a–c**. (Image courtesy of Dr. Georges Salamon.) Note that the increased contrast enhancement in **b** compared to **a** originates from the phase contrast shown in **c**. These images were collected at 3.0T.

Chapter 3

Apparent Voxel Phase

Chapter 3 is an article published in Journal of Magnetic Resonance Imaging. Xu Y and EM Haacke, The role of voxel aspect ratio in determining apparent vascular phase behavior in susceptibility weighted imaging, *MRI*, 2006, 24:155-160.

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**The Role of Voxel Aspect Ratio in Determining Apparent Vascular Phase
Behavior in Susceptibility Weighted Imaging**

Yingbiao Xu^{1,2} and E. Mark Haacke^{1,2}

¹Wayne State University

²The MRI Institute for Biomedical Research

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Corresponding author:

Yingbiao Xu

440 E. Ferry Street, Unit 2

Detroit, MI 48202

313-758-0065 tel

313-758-0068 fax

Abstract

Susceptibility weighted imaging (SWI) uses apparent phase contrast to enhance the contrast-to-noise ratio in the magnitude image. In theory, the apparent phase will depend on the aspect ratio when both venous blood and parenchyma occupy the same voxel. To demonstrate the maximal expected effect of the external field from a vein, we model the vein as an infinitely long cylinder perpendicular to the main magnetic field. The results show that the apparent phase of a voxel in the image is a function of resolution, vessel size and to a lesser degree vessel center within the voxel. The simulations explain why a negative phase mask has worked in SWI (1) processing of high resolution images collected in the transverse direction, despite the expected positive phase behavior for vessels perpendicular to the main field. The predicted phase behavior from the simulations is in good agreement with that observed from human brain datasets.

Introduction

Susceptibility weighted imaging (1) utilizes relative magnetic susceptibility differences between tissues of interest and the background or surrounding tissues to enhance image contrast (2-4). It is becoming a more and more important clinical tool and understanding the mechanisms behind the contrast generated is critical to its proper implementation and to the Radiologist's interpretation of the results. The susceptibility difference between deoxygenated blood and oxygenated blood in the brain results in excellent contrast between veins and gray or white matter in the phase image (5-8). The algorithm to enhance the contrast involves applying a high pass filter (9) to remove the low spatial frequency components of the background local field. The resulting filtered phase image $\varphi(x)$ is used to create a "phase" mask that, in turn, is used to multiply the original magnitude image to enhance the contrast between tissues. The phase mask can either be $f(x) = (\varphi(x) + \pi)/\pi$ if $\varphi(x)$ is negative and unity if $\varphi(x)$ is positive or $f(x) = (\pi - \varphi(x))/\pi$ if $\varphi(x)$ is positive and unity if $\varphi(x)$ is negative. The former is referred to as the negative phase mask while the latter is referred to as the positive phase mask. The number of multiplications of the phase mask into the original magnitude image turns out to be 4 or 5 to achieve the optimal $CNR/\sqrt{\text{time}}$ (1). Practically, SWI scans are usually run in a transverse orientation and a negative phase mask is applied to enhance the CNR in the magnitude images. In this paper, we examine the apparent voxel phase as a function of resolution and vessel size.

Theory

While phase is a linear function of echo time, the apparent phase of a voxel can also be a function of the resolution when the tissue of interest is a small object such as a vein and the voxel contains more than one tissue. For a voxel containing only a vein, i.e., a one compartment model, the phase, ϕ , develops according to the simple linear formula

$$\phi = -\gamma\Delta B \cdot TE \quad (1)$$

where γ is the magnetogyric ratio of protons, ΔB is the field difference between blood and the background, and TE is the echo time at which the data are sampled. Consider an infinitely long, cylinder-like vessel perpendicular to the main magnetic field with a diameter less than the in-plane resolution. Including any tissue surrounding the vessel in the pixel creates a two compartment model. For the intra-vascular field, the magnetic field difference ΔB_{in} can be written (2-4) as

$$\Delta B_{in} = -4\pi\chi_{do}B_0(1-Y)Hct / 6 \quad (2)$$

where $\chi_{do} = 0.18 \times 10^{-6}$ is the susceptibility change between de-oxygenated and oxygenated blood, B_0 is the main static field strength, Y is the fractional oxygen saturation of the blood in the vessel, and Hct is the fractional haematocrit (10,11).

For the extra-vascular field, the field difference ΔB_{out} can be written as

$$\Delta B_{out} = 4\pi\chi_{do}\cos 2\phi(r^2/\rho^2)B_0(1-Y)Hct/2 \quad (3)$$

where ϕ is the polar angle between the position P in the voxel and the projection vector of the main field B_0 onto the plane perpendicular to the vessel axis (the

plane of which also contains P), r is the radius of the vessel and ρ is the distance of the position P to the center of the vessel.

Materials and Methods

To obtain an accurate estimate of the magnitude and phase for the two compartment model of vein and parenchyma, we simulate the signal from a vessel perpendicular to the main magnetic field and the signal in the surrounding voxels containing only parenchyma. Our approach is to break up each voxel into a set of sub-voxels in which the signal is determined numerically. Specifically, we create an image covering a region of interest demarcated by the rectangle abcd in Fig. 1a with 512×512 pixels (the sub-voxels each have the same width and height of one unit. The voxel location and dimensions (height h and width w) are shown by the rectangle pqrs in Fig. 1a. The units for w , h and vessel diameter R are expressed in terms of the sub-pixel unit which is one by choice. The vessel cross section (the circle in Fig. 1a) is perpendicular to the image plane and the vessel's origin is at the center of the image. The vessel has a diameter of R units, which is set to be large enough to reduce numerical error. The vessel and surrounding tissues are given the same magnitude. Note that the relative vessel volume fraction depends on the inverse of the product of w times h . Fig. 1b shows a simulated phase image based on Eq. 1-3 along with the superimposed voxel.

By complex averaging the signal from each sub-voxel in the window of w by h units, we can simulate the signal of each image voxel. The phase and magnitude of the voxel containing the vessel are simulated with the vessel located at the center of the window. The phase and magnitude profiles of adjacent voxels (also of height h and width w) are simulated by sliding the rectangle window in either the through-plane or in-plane direction. The sliding step is chosen to be half of the window height or width to give an interpolated profile. The resulting phase profile gives an indication of the case when the vessel is not perfectly centered in the voxel. The magnitude profiles are multiplied by the phase mask four times (1) to see the effectiveness of the phase mask and any artifacts associated with the phase mask multiplication. For the simulation, we assume the main magnetic field is along the vertical direction as shown in Fig. 1.

To compare the simulation results with actual data, high resolution 3D datasets of a human brain were acquired in the transverse orientation on a 4T Bruker MED-SPEC system (Ettlingen, Germany) equipped with a Siemens Sonata (Erlangen, Germany) interface with different resolutions: $0.5 \times 0.5 \times 1 \text{ mm}^3$, $1 \times 0.5 \times 1 \text{ mm}^3$, and $0.5 \times 1 \times 2 \text{ mm}^3$. Segments of vessels that run predominately in the horizontal or vertical direction were located and the phase of the vessels was measured. A fully velocity compensated 3D gradient echo sequence was used with an echo time 15 ms and a repeat time 29 ms.

Results

Figure 2 shows that for relatively short TE (less than 15 ms), and w less than h , (with $w=R$) the apparent voxel phase is negative and has a nearly linear behavior as a function of TE. For a fixed TE, and TE less than 15 ms, the absolute value of the negative phase peaks when the ratio of h to w is about 4. Figure 3 shows the apparent voxel phase as a function of TE and vessel volume fraction by holding w and h fixed ($w:h=1:4$) and shrinking the vessel diameter R . The apparent voxel phase is negative for all cases shown. As the volume fraction decreases for a fixed TE, so does the apparent voxel phase. This observation indicates that high resolution is necessary for the phase mask to be effective when the interest is to see small veins. The apparent voxel phase shows better linearity as a function of TE when the volume fraction is low. Fig. 2 and Fig. 3 correspond to the more traditional voxel aspect ratio used in a transverse acquisition (by traditional we mean the resolution in slice thickness is lowest). Figure 4 is more representative of a traditional coronal or sagittal scan plane. In this situation, the apparent voxel phase is only positive (assuming no aliasing occurs). As the ratio of width to height increases, the apparent voxel phase decreases since the volume fraction decreases.

Figure 5a gives the in-plane profiles of apparent voxel phase perpendicular to the vein for the case when the height (h) is larger than or equal to the width (w) of the voxel. (This is similar to the conventional transverse plane acquisition.)

Figure 5b and 5c are in-plane profiles of magnitude without and with phase multiplication (negative phase mask), respectively. Figure 5a shows that the phase of the center voxel goes from positive to negative as the ratio of height over width increases (slice thickness increases in the traditional transverse acquisition case). The phase of the voxel one voxel away from the center voxel remains positive. These results make the choice of a negative phase mask mandatory if one does not wish to create an artificial increase in the apparent vessel size. Without phase multiplication to enhance contrast (Fig. 5b), the higher the resolution, the larger the volume fraction and the bigger the signal cancellation of the voxel that contains the vein. The signal loss of the adjacent voxels is less than 10%, so if the signal loss in the central voxel is much higher, it will not appear as if the vein is broadened.

Figure 6a is a plot of the phase profile in the through-plane direction perpendicular to the vein when the height is larger than or equal to the width of the window. Figure 6b and 6c are the corresponding magnitude profiles without and with phase multiplication, respectively, using the negative phase mask. From Fig. 6a, the apparent phase of the voxels one voxel away from the center voxel are all negative. Without phase multiplication, there is no signal loss through-plane one voxel away (or on the adjacent slice, Fig. 6b). With 4 times phase multiplication (Fig. 6c), the ratio of in-plane to through-plane resolution 1:4 is

avored not only to result in a larger signal cancellation but also to reduce the unwanted signal cancellation on adjacent slices.

Figure 7a and 7b are examples from a human brain. The data was acquired on the 4T Bruker MED-SPEC system (Ettlingen, Germany) system. Both images have the same resolution 1 (phase encoding) x 0.5 (readout) x 2 (slice select) mm³. The only difference between the two acquisitions is the readout direction. For the image on the left, the readout is in the vertical direction while for the image on the right the readout is in the horizontal direction. Notice that most of the big veins are well delineated in both images. However, for a vein predominantly running along the vertical direction, it is much sharper in Fig. 7b than in Fig. 7a (horizontal arrow). The same vein is barely seen in Fig. 7a. The vein in Fig. 7b (horizontal arrow) has higher in-plane resolution (the ratio of height over width is 4) than that of Fig. 7a (the ratio of height over width is 2), hence the larger the volume fraction the larger the phase. The same is true for the vein indicated by the vertical arrow. Now the vein is sharper on the left image than on the right image because the left image has higher in-plane resolution across the vein.

Figure 8 is a measured profile of the phase through-plane near one vein perpendicular to the main magnetic field from a human brain. The profiles are in line with the predictions from the simulations (Fig. 6a) in terms of the sign of the

apparent phase of the voxel which changes from positive to negative when the slice resolution increases. However, the measured phases have a larger amplitude than the ones predicted. Finally, to demonstrate the phase behavior in humans, Figure 9 contains two high resolution in plane *in vivo* phase images. The veins (see arrows) show the expected phase behavior of negative in the transverse image (R:w:h = 1:1:4) versus positive in the sagittal image (R:w:h = 1:2:1).

Discussion

Simulations were performed to evaluate quantitatively the role of the voxel aspect ratio for a vein perpendicular to the main field. It has long been known that high in plane resolution with a thicker slice is best for SWI images because all vessel phases appear negative. This is mandatory when one applies a negative phase mask so that excess vessel broadening does not occur. These simulations not only validate what has been previously understood but also make it possible to theoretically determine the best resolution to use in SWI. The simulations in Fig. 2 to 4 show that the phase of the voxel containing the vessel is a function of resolution (hence acquisition orientation) and vessel size.

When viewed analytically, with no partial volume effects, the phase from the vessel itself is positive for a vein perpendicular to the main magnetic field. However, the apparent phase of the voxel is the argument of the integration of the complex signal over the two compartments (one is the vein itself and the other is

the parenchyma surrounding the vein). The phase outside the vein is modulated by the $\cos 2\phi$ term. For a conventional transverse acquisition (w less than h), the apparent phase of the voxel is negative (Fig. 9a). This is because the thick slice basically integrates along a line directly above the vessel where the angle ϕ is close to zero. This long thin voxel is then dominated by a negative phase behavior while the adjacent voxel has net positive phase (Fig. 9a). On the other hand, a conventional sagittal acquisition results in a positive phase for the voxel containing the vein and negative phase for the in-plane voxels adjacent to it (Fig. 9b). This partial volume effect shows that the apparent phase of a voxel depends on both the imaging resolution and the voxel location relative to the vein. The highest negative phase is seen when the aspect ratio of the voxel is such that the voxel dimension parallel to the main field is about 4 times the voxel dimension perpendicular to the field.

Other angles of the vein to the main field were not considered since the largest extravascular effect occurs for the vein perpendicular to the main field. Still, one might expect a similar behavior in terms of creating a negative phase but less dramatic because of the reduced extravascular field as the angle of the vein to the main field decreases. Finally, as the angle goes to zero, the phase inside the vessel has become strongly negative on its own.

Figure 7a and 7b show that the highest in-plane resolution should be along the direction orthogonal to the long axis of the vein. Practically, veins run in all directions as seen in Fig. 7. The best results would clearly be to collect a 512 x 512 image highlighting all vessels. (This has actually been demonstrated by Reichenbach et. al (5) where images with both 512 x 512 and 1024 x 1024 matrix size were collected).

Figure 5 predicts that the R:w:h = 1:1:2 case has the best cancellation effect. In practice, we find that the 1:1:4 case gives much better visual effects. This is probably due to the fact that the CNR of the former is one-half that show in the theoretical prediction of signal loss which does not account for noise.

Conclusions

A careful understanding of the phase behavior has been shown to predict why the transverse acquisition is perhaps the best way to collect susceptibility weighted imaging data when the main field is along the long axis of the body. The results show that for a vessel perpendicular to the main magnetic field that the phase is a function of vessel size and imaging resolution. The predictions are in good agreement with the observations in human brain datasets. The results suggest that the best aspect ratio to use for SWI imaging is R:w:h = 1:1:4. Therefore, if it is the small veins of 0.5mm in size that are of interest, this implies for a transverse

acquisition that an in-plane resolution of 0.5mm x 0.5mm with a slice thickness of 2mm will yield the best results.

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References

1. Haacke EM, Cheng Y.N, Xu Y, Reichenbach J.R, Susceptibility Weighted Imaging, *MRM* 52, 612-618, 2004.
2. Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci USA* 1990; **87**: 9868-9872.
3. Ogawa S, Lee TM. Magnetic resonance imaging of blood vessels at high fields: in vivo and in vitro measurements and image simulation. *Magn Reson Med* 1990; **16**: 9-18.
4. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magn Reson Med* 1990; **14**: 68-78.
5. Reichenbach JR, Venkatesan R, Schillinger DJ, Kido DK, Haacke EM. Small Vessels in the Human Brain: MR Venography with Deoxyhemoglobin as an Intrinsic Contrast Agent. *Radiology* 1997; 204:272-277.
6. Reichenbach JR, Barth M, Haacke EM, Klarhöfer M, Kaiser WA, Moser E. High-Resolution MR Venography at 3 Tesla. *JCAT* 2000; 24:949-957.
7. Reichenbach JR, Jonetz-Mentzel L, Fitzek C, Haacke EM, Kido DK, Lee BCP, Kaiser WA. High-Resolution Blood Oxygen-Level Dependent MR

- Venography (HRBV): A new Technique. *Neuroradiology* 2001; 43:364-369.
8. Reichenbach JR, Haacke EM. High-Resolution BOLD Venographic Imaging: A Window into Brain Function. *NMR in Biomedicine* 2001; 14:453-467.
 9. Wang Y, Yu Y, Li D, Bae KT, Brown JJ, Lin W, Haacke EM. Artery and vein separation using susceptibility –dependent phase in contrast-enhanced MRA. *JMRI* 2000; 12:661-670.
 10. Weiskoff RM, Kiihne S. MRI Susceptometry: Image-Based Measurement of Absolute Susceptibility of MR Contrast Agents and Human Blood. *MRM* 1992; 24:375.
 11. Haacke EM, Brown RW, Thompson MR, Venkatesan R. Magnetic Resonance Imaging, Physical Principals and Sequence Design. New York:Weily-Liss; 1999. p 741-771.
 12. Rauscher A, Barth M, Reichenbach JR, Stollberger R, Moser E. Automated unwrapping of MR phase images applied to BOLD MR-venography at 3 Tesla. *JMRI* 2003; 18:175-180.

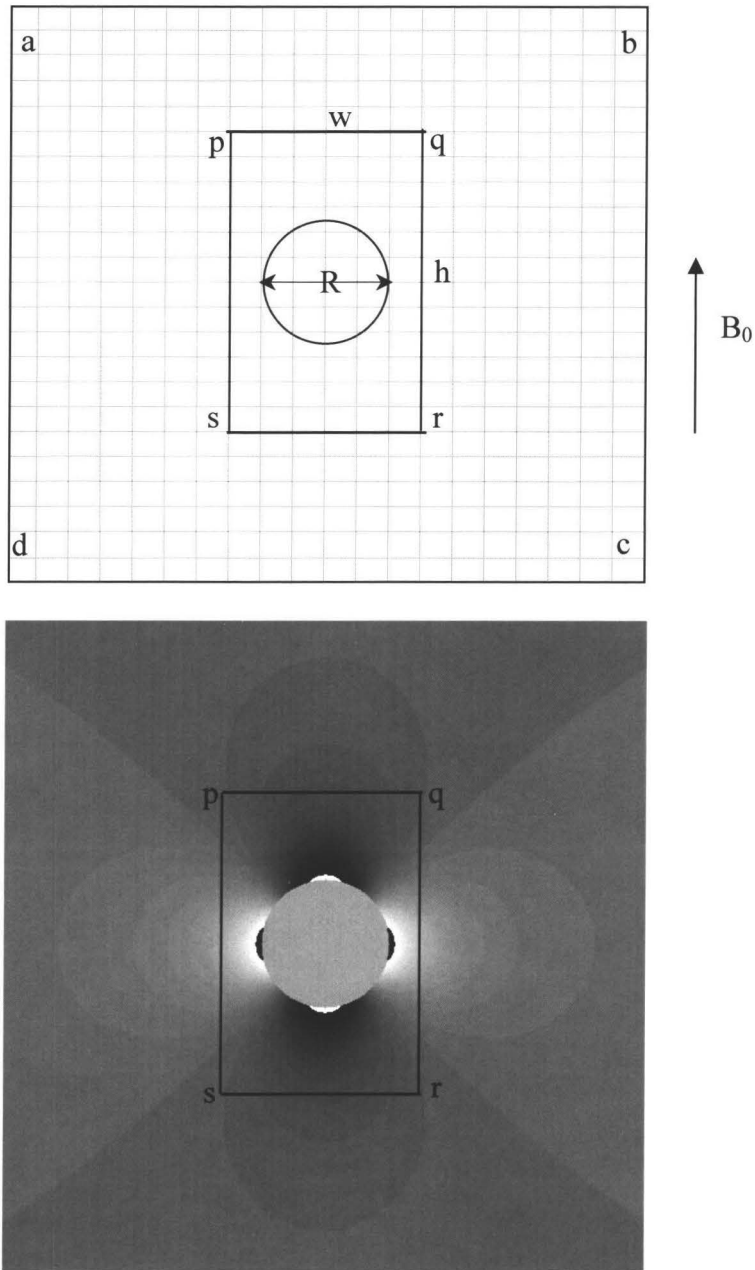


Figure 1a) The rectangle region $abcd$ represents the area surrounding the vessel (the circle in the middle), which is perpendicular to the main magnetic field B_0 . This area is divided into 512 by 512 sub-voxel fine grids to simulate the phase

numerically. The rectangle region $pqrs$ ($pq=w$, $qr=h$) represents the voxel that contains the vessel. The apparent phase of the image voxel is calculated from a complex average of the sub-voxels in the rectangle region $pqrs$. By sliding $pqrs$ in either the horizontal or vertical directions, we can calculate the response profiles in either an in-plane or through-plane case. 1b) Simulated phase image for the vessel shown in 1a). While phase within the vessel is positive, the phase outside the vessel varies. The apparent phase of the voxel clearly depends on the resolution (represented by the rectangle region $pqrs$).

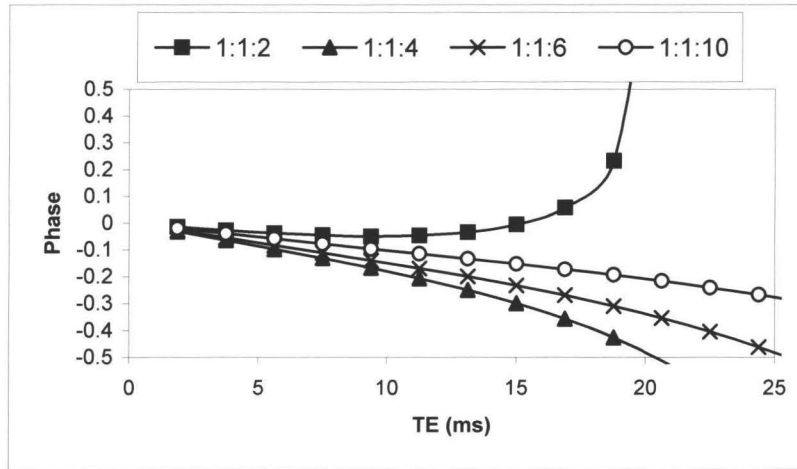


Figure 2: shows the phase of the voxel as a function of the ratio of R:w:h and TE. The width of the window, w, equals the vessel diameter R. Note, for fixed TE, the negative phase peaks when the ratio of h to w is about 4. Also the phase is almost a linear function of TE when TE is less than 15 ms.

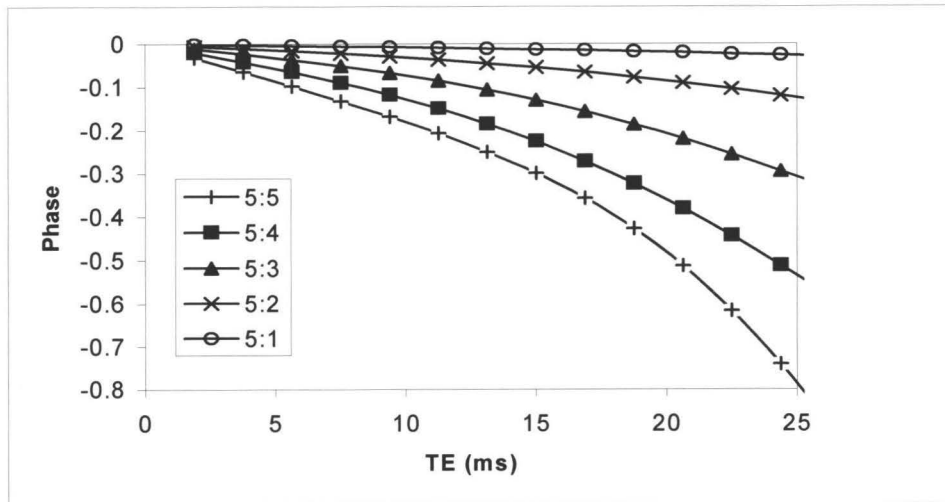


Figure 3 shows the phase of the voxel as a function of the ratio of w to the vessel diameter R and TE . The ratio of h to w (see Fig. 1) is set to be 4:1. Note, for fixed TE , the smaller the ratio of w to the vessel diameter, the larger the phase, which indicates that high resolution is necessary for the phase mask to be effective to enhance small vessels.

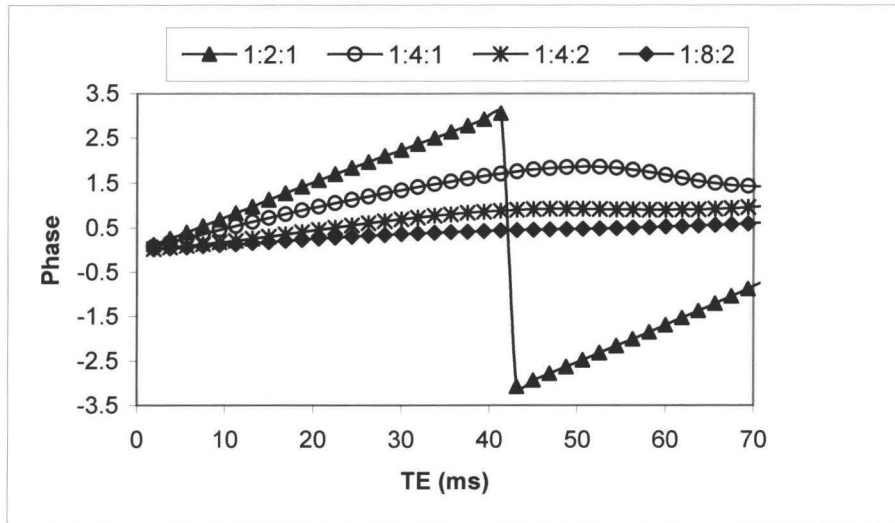


Figure 4: Phase of the voxel as a function of the ratio of R:w:h and TE. Note, the phase is positive when there is no aliasing.

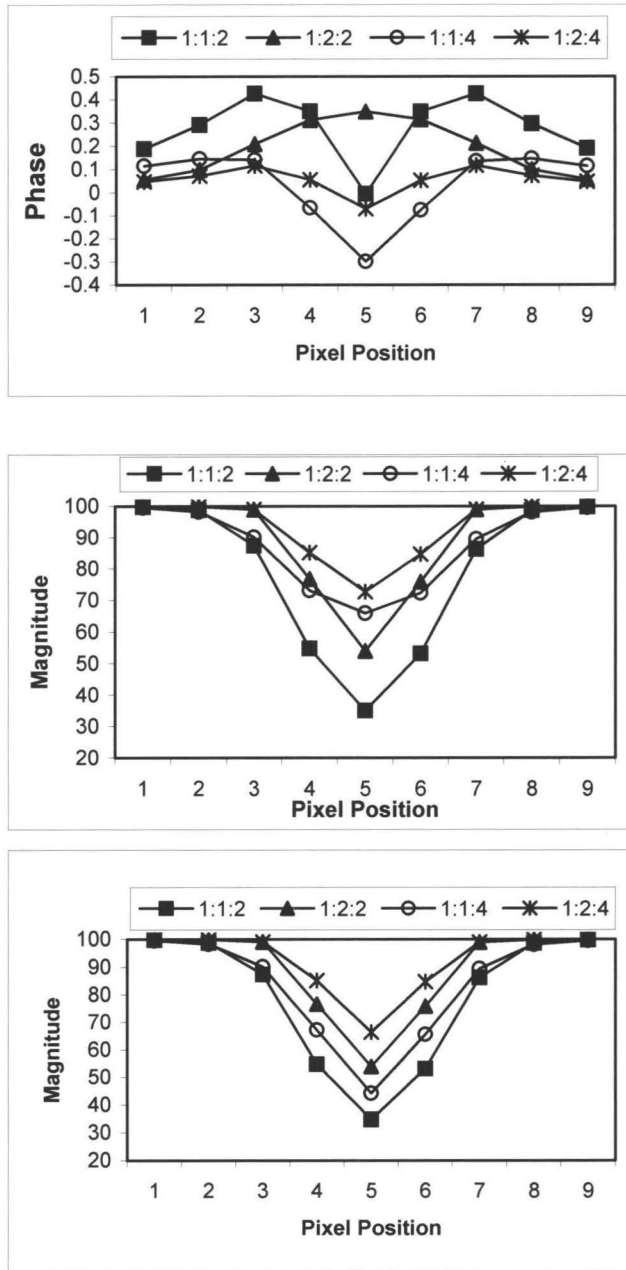


Figure 5: Transverse acquisition. a) In-plane phase profiles perpendicular to the vessel at TE 15 ms for different ratios of R:w:h. The center of the vessel is located at the center of the profile. One unit on the pixel position axis represents half of the pixel width (w). b) Corresponding in-plane magnitude profiles without any phase mask multiplication. The magnitude is normalized to be 100 when there is no signal cancellation. c) In-plane magnitude profiles after multiplying 4 times with the negative phase mask.

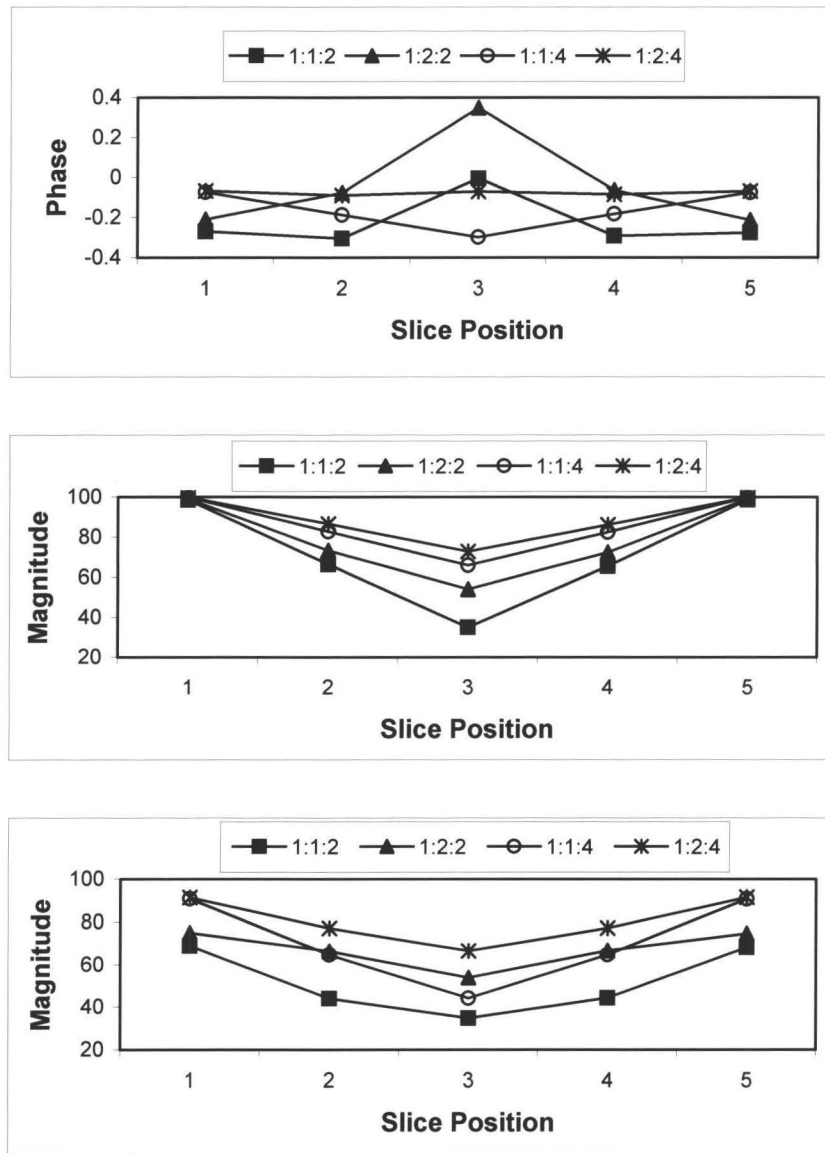


Figure 6: Transverse acquisition. a) Through-plane phase profiles perpendicular to the vessel at TE 15 ms for different ratios of R:w:h. The vessel is located at the center of the profile. One unit on the slice position axis represents half of the slice thickness (h). b) Corresponding through-plane magnitude profiles without any phase mask multiplication. The magnitude is normalized to be 100 when there is no signal cancellation. c) Through-plane magnitude profiles after multiplying 4 times with the negative phase mask.

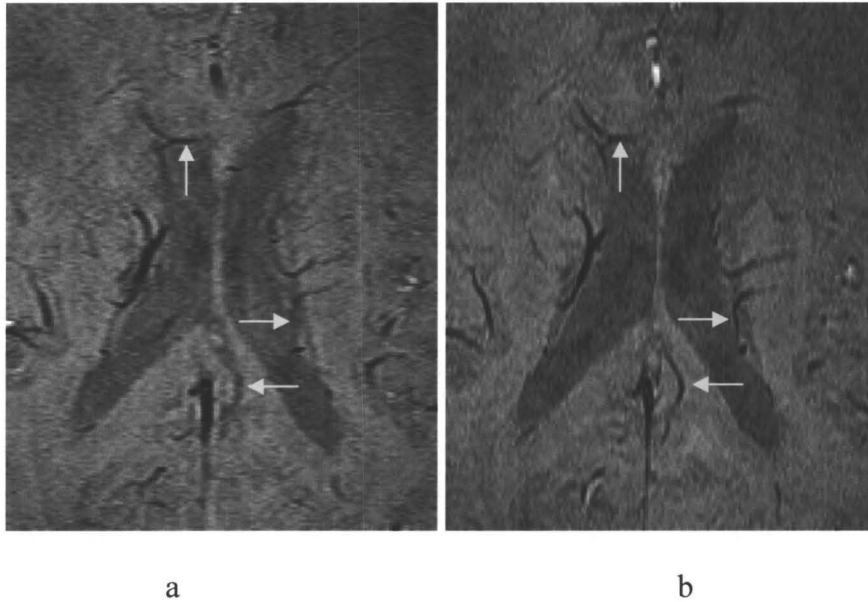


Figure 7: a) SWI image with 4 times phase mask multiplication. In-plane resolution 1mm x 0.5 mm (horizontal verses vertical) while the through-plane resolution is 2mm. b) The same as a) except the in-plane resolution is 0.5mm x 1mm. Note, the vessels running predominately along vertical direction are much sharper in Fig. 7b) (horizontal arrows), While the vessels running along the horizontal direction are better shown in Fig. 7a) (vertical arrow). Both Fig. 7a and 7b show the ratio of 1:4 (in-plane (w) verses through-plane (h) resolution) results better signal cancellation than ratio of 2:4 as predicted in Fig 5c) for small vessels. These images show that the choice of resolution is critical in revealing small vessels.

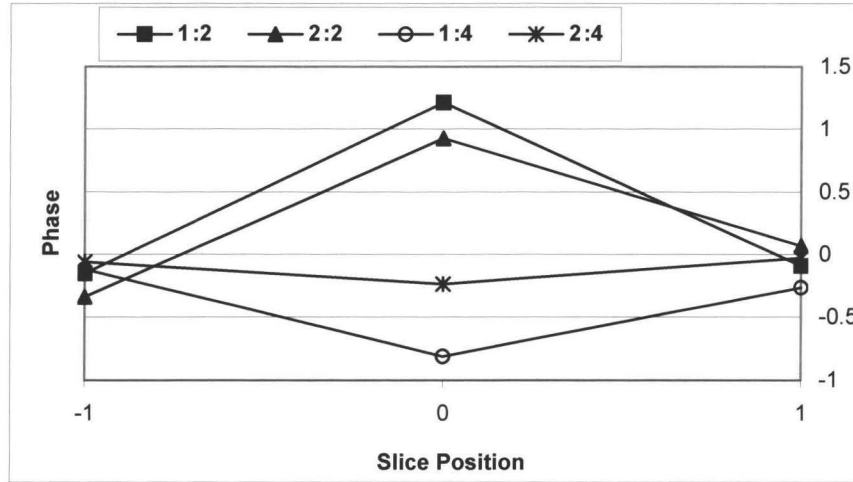


Figure 8: Measured phase profiles in the through-plane direction for a vessel running in the A to P direction perpendicular to the main magnetic field as a function of in-plane to through-plane resolution ratio. (These profiles come from a high resolution 3D data set acquired in transverse orientation as described in the text.) Each profile covers three slices with the center slice (slice position 0) containing the vessel. Note: the phase from the center slice changes from positive to negative when the through-plane resolution doubles and the phases are still negative for adjacent slices (in agreement with the predictions of Fig. 6a). The small value of adjacent slice phases implies that there will not be significant overestimation of the vessel size outside the pixel of interest.

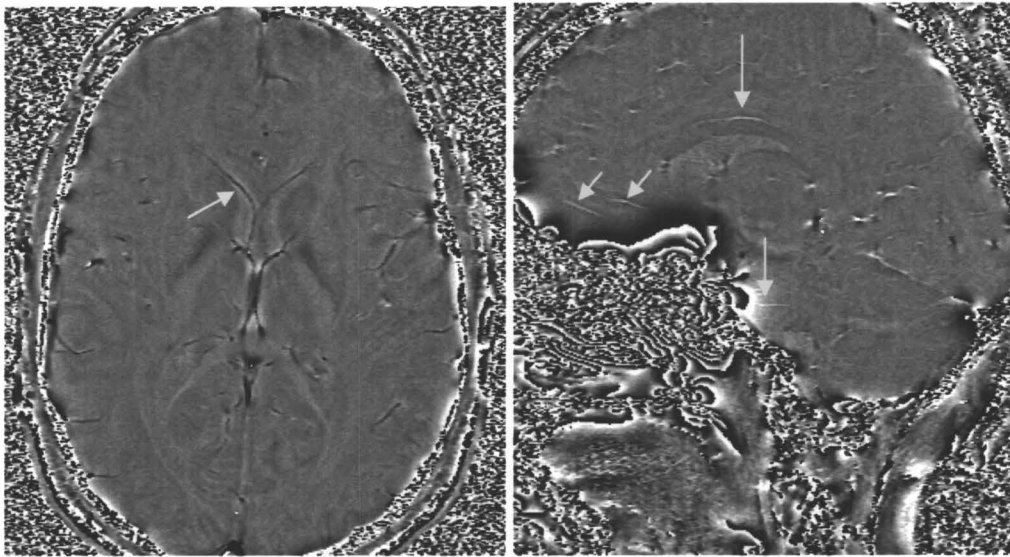


Figure 9: Two *in vivo* phase images. The left image (from a transverse acquisition with a resolution of $1 \times 0.5 \times 2 \text{ mm}^3$) shows the negative phase for small vessels perpendicular to the main field as predicted by the simulations. The right image (from a sagittal acquisition with a resolution of $1 \times 0.5 \times 1 \text{ mm}^3$) shows the expected positive phase for vessels nearly perpendicular to the main field. The arrow in the left image shows the septal vein while the arrows in the right image show a number of veins now positive due to their orientation and sagittal acquisition.

Chapter 4

Geometric Distortion Corrected Segmented EPI

(GDC-SEPI) Sequence

(Chapter 4 consists of material submitted to the Journal entitled Magnetic Resonance Imaging, which is currently under review process after revision.)

**An Iterative Reconstruction Technique for Geometric Distortion Corrected
Segmented EPI (GDC-SEPI)**

Yingbiao Xu^{1,2} and E. Mark Haacke^{1,2}

¹McMaster University, Hamilton, Ontario, ²Wayne State University, Detroit,
Michigan

Key words: segmented echo planar imaging, iterative phase correction, center out
k-space trajectory, GDC-SEPI

Corresponding author:

Yingbiao Xu

440 E. Ferry Street,

Detroit, MI 48202

Phone: (313)7580065

Email: am4229@wayne.edu

Abstract

In this paper, we introduce a simple and efficient technique to phase correct Segmented Echo Planar Imaging (SEPI) data in the presence of moderate field inhomogeneities. This phase correction reduces the distortion in the phase encoding direction without requiring an extra reference scan. Using a center out k-space trajectory and a low spatial frequency phase map, phase discontinuities between segments can be eliminated iteratively using a fast Fourier transform from the center segment to the outermost segment in k-space. With an extra echo added in front of the echo train, neither phase unwrapping nor an extra reference scan is required to obtain a low spatial frequency phase map. The method is shown to remove blurring and reduce geometric distortion caused by phase changes from echo to echo in both phantom and human data. The method is most useful for high resolution imaging applications and moderate factors of speed improvement.

Introduction

Multi-shot or segmented echo planar imaging (SEPI) offers higher resolution and better off-resonance behavior compared with single shot EPI. Since the inception of EPI in 1977 [1] and segmented EPI in 1986 [2], the main challenges have been to remove off-resonance effects from background field effects and correct for non-ideal sampling. Improved gradients and calibration techniques along with the echo time shifting (ETS) technique [3] effectively eliminate ghosting or blurring caused by the phase discontinuity between segments. However, the distortion caused by off-resonance phase errors in the phase encoding direction remains fairly large. There are even special applications in magnetic resonance angiography (MRA) [4,5] or in susceptibility weighted imaging (SWI) [6] when only even or odd echoes are sampled to maintain special flow properties such as motion compensation. With increased inter-echo spacing, distortion also increases. Field mapping methods [7-9] can effectively reduce image distortion originating from off-resonance effects such as B_0 field inhomogeneity and chemical shift. The field map is derived usually from phase information obtained from either a double-echo gradient echo or offset spin-echo images. However, the phase residual derived from different echo times has to be unwrapped to get the field inhomogeneity map [10]. Using multiple reference scans [11] and multi-echo gradient-echo imaging [12] makes it possible to reduce B_0 field inhomogeneity effects more accurately by eliminating eddy current effects. Chen and Wyrwicz [13] further developed a phase shifted EPI pulse sequence that takes

into account all off-resonance effects including gradient waveform imperfections and their method does not require phase unwrapping. Finally, there are brute force approaches using the generalized inverse transform to perform off-resonance correction and attempts to speed these up by using fast conjugate phase reconstruction (CPR) algorithms [14,15]. The approach we take can account for phase variations between echoes caused by arbitrary moderate 2D spatial field inhomogeneities. Although we focus on the use of phase from the central part of k-space, the method works even better when an accurate high resolution phase image is available. Given the rapid scanning possible today, it is not excessive to imagine having the full phase information to use in future applications.

Theory

It's well known that the off-resonance artifact mainly manifests itself as distortion when Cartesian k-space trajectories are used [14]. In this paper, we ignore the phase error term related to the readout direction because the bandwidths used are usually very large [8,12]. The segmented data collection scheme is shown in Fig. 1. Only the even echoes are sampled. In our approach, the center of k-space is sampled first. Ignoring the relaxation effects, the sampled k-space data,

$s(m\Delta k_x, n\Delta k_y, l\Delta T)$, with the matrix size $N_x \times N_y$, can be represented as (for a left handed system)

$$s(m\Delta k_x, n\Delta k_y, l\Delta T) = \iint \rho(x, y) \exp(im\Delta k_x x) \exp(in\Delta k_y y) \exp(i\phi(x, y, l\Delta T)) dx dy$$

(1)

$$-N_x/2 \leq m < N_x/2, \quad -N_y/2 \leq n < N_y/2$$

where $\rho(x, y)$ is the spin density of the scanned object, ΔT is the inter-echo time interval (i.e. the time duration between two consecutive even echoes), l is the echo index on the echo train (see Fig. 1) (l is implicitly a function of n). In Eq. (1), l starts from 1 because the data sampled on the first echo is not used to fill k-space (see Fig. 2). Also, l corresponds to the segment number labeled in Fig. 2, and $\phi(x, y, l\Delta T)$ is the phase error. This phase term originates from off-resonance effects and is related to the phase evolution in the phase encoding direction as follows:

$$\phi(x, y, l\Delta T) = i\omega_0(x, y)(l\Delta T + TE(0)) \quad (2)$$

where $\omega_0(x, y) = \gamma\Delta B(x, y)$ is representative of the local field inhomogeneity and $TE(0)$ is the echo time of the first echo in the echo train.

A formal means to compensate for the phase accrual due to local field inhomogeneities is to multiply each sampling point in k-space by the phase conjugate of the inhomogeneity accrued:

$$\hat{\rho}(x, y) = \sum_m \sum_n S(m\Delta k_x, n\Delta k_y, l\Delta T) \exp(-im\Delta k_x x) \exp(-in\Delta k_y y) \exp(-i\phi(x, y, l\Delta T)) \quad (3)$$

The difficulty in a straight forward implementation of this method is that a Fourier transform of the corrected data must be applied for each (x,y) point. This is tantamount to having performed a generalized inverse transform in terms of the

processing it would take to reconstruct the entire object. The main objective of this paper is to show that this problem can be solved easily and quickly with a unique iterative Fourier transform approach between k-space and the imaging domain.

Materials and Methods

Sequence design

Figure 1 shows the sketch of the proposed 2D sequence diagram with a turbo segmented factor (TSF) of 4. Again only the even echoes are sampled. One unique feature is that one additional echo is added to the beginning of the normal echo train. The first echo (the additional echo) has the same encoding as the second echo. This makes it possible to derive a phase map from these two echoes. The phase map derived from the first two echoes can be applied directly to later echoes without phase unwrapping. With high resolution (say 256 or more k-space lines) and a TSF of, say, 4 for 256 lines (or more for a larger matrix), the central k-space region (or segment 1) is large enough practically to give a good estimate of the phase map. The phase evolution $\varphi(x, y)$ between the first and second echoes is a linear function of $\omega_0(x, y)$, and echo spacing ΔT ,

$$\varphi(x, y) = \omega_0(x, y) \Delta T \quad (4)$$

This phase continues to evolve from echo to echo with the same functional form.

Figure 2 is the sketch of a 2D k-space collected with a four-echo segmented EPI sequence with a center out trajectory. The number of each shaded region corresponds to a given segment of k-space (for a specific echo). With 256 k-space lines, it takes 32 radio-frequency (RF) pulses to cover each region within a given segment. Except for the center of k-space (segment 1), there are two parts for each segment 2 through 4 (a top part and a bottom part). To show the order of acquisition of the k-space lines, we assume that the 2D k-space lines are indexed from 0 to 255 from bottom to top as an example. For the top half of k-space, the index of lines acquired with each RF pulse is

$$p = 127 + N_{rf} + 32 * (l - 1) \quad N_{rf} = 1, 2, \dots, 32; \quad l = 1, 2, 3, 4; \quad (5)$$

where p is the k-space line index, N_{rf} is the index of RF pulse and here l is the segment number (see Fig. 2). For the lower half of k-space,

$$p = 128 - N_{rf} - 32 * (l - 1) \quad N_{rf} = 1, 2, \dots, 32; \quad l = 1, 2, 3, 4; \quad (6)$$

The key observation here is that k-space data in the same segment is acquired at the same echo time and, therefore, has the same phase evolution pattern.

iterative reconstruction approach

The main idea in this paper is to take the data and merge it in a way that all data points have experienced effectively the same phase evolution, i.e., they act as if they were all collected at the same echo time. We do this by starting with the central part of k-space and modify its phase and then go through an iterative approach as described below to absorb all the different k-space regions collected.

Let L be the largest region index, then we multiply both sides of Eq. (3)

by $\exp(i\omega_0(x, y)L\Delta T)$

$$\hat{\rho}(x, y) \exp(i\omega_0(x, y)L\Delta T) = \sum_m \sum_n S(m\Delta k_x, n\Delta k_y, l\Delta T) \exp(-im\Delta k_x x) \exp(-in\Delta k_y y) * \exp(i\omega_0(x, y)(L - l)\Delta T) \quad (7)$$

Eq. (7) now serves as a guide in defining the iterative procedure. To correct from center out: first replace all data points in k-space in segments other than 1 with zero. Then Fourier transform the zero filled k-space to the image domain to get a complex image $\rho(x, y)$. Next multiply $\rho(x, y)$ with $\exp(i\phi(x, y))$ to get $\rho'(x, y)$. Then Fourier transform $\rho'(x, y)$ back to k-space and replace the data points in segment 2 with the original data points. This new k-space data is in theory the same as that which would have been acquired if all the data in both segment 1 and 2 had been collected at the third echo (i.e., the data points in segment 1 appear as if they had been collected at the same time as those in segment 2). There will be no phase discontinuity between segment 1 and 2 at this point. The next step is to let region 2' represent the merged k-space of both segment 1 and 2. The same procedure can now be applied to phase correct region 2' to eliminate the effect of the phase evolution between echo three and echo four and create a new k-space which appears as if it were all collected at the fourth echo. This method is continued one more time to correct for the phase evolution to the fifth echo. The final image will now appear to have been acquired (at least as far as phase effects

are concerned) at effectively one echo time, the final echo time. The proposed iterative reconstruction approach is also illustrated in the flow chart in Fig. 3.

Simulation

For the segmented EPI, the currently accepted technique is the echo time shifting (ETS) method [3]. ETS effectively reduces the k-space discontinuities between k-space lines. The ETS method helps reducing imaging artifacts such as ghosting, blurring and Gibbs ringing but image distortion still remains. Combining the center out k-space trajectory and ETS not only doubles image distortion compared with the bottom-up k-space trajectory but also adds additional distortion in the opposite direction. Figure 4 shows the distortion artifacts related to the center out k-space trajectory and ETS with both phantom simulation as well as an *in vivo* acquisition. Fig. 4b and Fig. 4d are simulated segmented EPI images with ETS and the center out k-space trajectory, respectively. The resolution phantom (Fig. 4b) indicates that ETS is not a suitable method for center out k-space trajectory approach since the double-direction distortion makes a mess of smaller structures. Both the oil/water phantom (Fig. 4d) and the *in vivo* image (Fig. 4e) show a large fat shift in both directions. Obviously the overlay of shifted fat signal on the brain parenchyma (pointed by yellow arrows) creates bad artifacts.

How well does the proposed method fare under different conditions such as smooth varying field like the resolution phantom or sharp field changes like

water/oil phantom? We simulated images using k-space datasets acquired with a multi-echo gradient echo sequence. The multi-echo sequence has fixed echo spacing so that we could reassemble k-space from a set of k-space lines coming from different echo times as if the reassembled k-space had been acquired with the proposed segmented EPI sequence with a center out k-space trajectory.

Figures 5 and 6 demonstrate that when the field is varying smoothly so that the phase map from the central k-space represents the phase reasonably well, the proposed GDC-SEPI method works superbly. Measured profiles (Fig. 5) indicate that the biggest residuals are actually still within the noise level. Fig. 6 shows the dramatically reduced coherent ringing as well.

In the case of rapid field changes such as shown in Fig. 7, central k-space isn't large enough to give a good estimation of the field at the boundary of the oil and water (Fig. 7c). Poor estimation of the phase results in signal loss at the boundaries (Fig. 7f). When we use the whole k-space to estimate the phase (Fig. 7d) then the signal loss get recovered (Fig. 7e). However, both Fig. 7e and 7f have the same ringing artifacts (caused by the T_2^* difference between oil and water). Accounting for phase variations from echo to echo doesn't correct the artifacts related to discontinuities in k-space caused by T_2^* decay. Further, Fig. 7a is a simulated SEPI image which shows a major fat shift along the phase encoding direction. Compared with Fig. 7a, the fat signal in both Fig. 7d and Fig. 7e doesn't

shift relative to the reference image. This demonstrates that the proposed method is accomplishing its goal of removing geometric distortion.

Image acquisition parameters

Both phantom and *in vivo* data were acquired on a Siemens Sonata (Erlangen, Germany) 1.5 T system. The phantom data is acquired with the following parameters: resolution $0.5 \times 1 \times 2 \text{ mm}^3$, 64 slices, the number of echoes in the readout echo train is 5, echo spacing (ΔT) = 8 ms, the echo time of the first echo = 10 ms, and TR = 51 ms. The *in vivo* data is acquired with a resolution = $1 \times 1 \times 2 \text{ mm}^3$, 64 slices, the number of echoes in the readout echo train = 5, echo spacing = 7.5 ms, the echo time of the first echo = 22.5 ms, and TR = 61 ms. The original raw data sets were downloaded to a PC for off-line image reconstruction and the proposed phase correction.

Results

Figure 8a is a phantom magnitude image reconstructed from the raw data acquired with the sequence shown in Fig. 1 without any phase correction. The largest resolution circle is reasonably well delineated with the central k-space region alone. The phase discontinuities between echoes cause severe artifacts including: distortion, ghosting and blurring for the small resolution circles. Figure 8b and 8c are the intermediate results after the first and second iterations of the proposed phase correction, respectively. Figure 8d is the result after the final iteration of the

phase correction. From Fig. 8b, 8c to 8d, we see continued improvement of the image quality, although the majority of the improvement comes after the first iteration. Further effects refine the higher resolution components as expected but only to the degree that the central phase correctly estimates the high resolution phase behavior. After the full correction, geometric distortion, ghosting and blurring are mostly gone, which indicates a successful reduction of the effects of phase evolution between echoes. However, the correction is not perfect in the area of the smallest circles. There are residual ripples that are the result of missing high frequency information in the phase map. There is also some remnant low spatial frequency Gibbs ringing present.

Part of the motivation for this work was the need to obtain susceptibility weighted images that first could be acquired quickly at 1.5T and second would appear to be flow compensated for arterial flow. To demonstrate that this is possible, we used the sequence shown in Fig. 1 to acquire raw data *in vivo* for a neuro-imaging example. For SWI we need a longer echo time [4], so we began the sequence with the first echo time of 22.5 ms with echo spacing of 7.5 ms. With a TSF of 4, this sequence only took about 4 minutes to cover 64 slices (whole brain coverage) instead of the usual 16 minutes. Figure 9a is a magnitude image reconstructed simply with the usual Fourier transform without any phase correction. Blurring is seen throughout the image especially where there is fat. Figure 9b is a magnitude image reconstructed after the proposed phase correction.

Fig. 9b shows the improvement in the sharpness of the image. To show the improvement with the iterative phase correction technique, two residual images (Fig. 9c and 9d) between Fig. 9a and Fig. 9b are displayed as well. Fig. 9c reveals that the dominate residual error is in the neighborhood of fat signal. Fig. 9d only shows the area of brain parenchyma in order to appreciate the improvement of fine structures in the brain. Fig. 9e is a magnitude image acquired with a conventional SWI sequence (with TE/TR = 40/57 ms) (which took about 8 minutes to cover only 32 slices or half of the brain) and serves as a reference image here. For the conventional SWI image, arterial and venous signals are naturally separated with arterial signal being bright and venous signal being dark. Fig. 9f is a magnitude image acquired with a Siemens segmented EPI sequence. Both arteries and veins appear dark in Fig. 9f. This makes separating arteries and veins problematic. The center out k-space acquisition used to acquire Fig. 9b leads to bright arteries and dark veins as expected and produces similar contrast to that seen with conventional SWI.

Discussion

The results shown here represent an improvement in image quality for segmented EPI when the number of segments is small and the matrix size is large. The method is fast, requires no phase unwrapping and no extra reference scan and should be easily implemented online. However, there is a trade off between the TSF and the accuracy of the phase map. Practically, this approach becomes better and better as the matrix size increases and the TSF remains the same. It is of

interest to note that one could use an extra reference scan to get an accurate high resolution phase map if time or motion between scans is not an issue. Under these circumstances, this iterative approach could be applied to SEPI data when both even and odd echoes are sampled. Further, it should improve the response for the smaller structures and fat signal which was not possible with the current implementation of the central k-space approach (see Fig. 9a and 9b).

For any high resolution, 3D imaging method, a small voxel size requires a fairly low bandwidth to ensure enough SNR. This implies that the TSF can't be too high otherwise the duration of the echo train would be too long and $T2^*$ filtering will become a problem. Of course, as with any segmented approach, one assumes that the subject does not move between scans. However, using more modern techniques such as propeller may make segmented methods more viable in the future [16].

Although we have performed the iterative procedure from the central data outwards, in principle this process could also be done from the outermost k-space toward the center. In practice, we found out that this approach wasn't as robust as the correction done from the center of k-space. The reason for this could be because the phase estimate from the center of k-space wasn't accurate enough to represent well the high spatial frequency components.

The overall improvement of the clinically relevant images may not be as evident as in the phantoms which have very sharp edges, but they are equally important. For example, Figure 9b has dramatically sharpened edges. This can be understood from the fact that the center of k-space already creates a reasonable albeit blurred low resolution image itself. This method attempts to correct the local blurring (which is actually a form of ghosting or aliasing that manifests as only small shifts of several pixels and hence can equally be called blurring). This blurring is another form of geometric distortion in this case, where it is most evident both in the fat and at air tissue interfaces like the edge of the brain. However, if these fine tuned corrections were not made, the result from Figure 9a would be unacceptable clinically. Therefore, the approach taken here has the potential to create high quality and clinically usable images when high resolution is the name of the game.

In fact, one of the key motivations for this segmented approach is the push for higher and higher resolution in anatomical imaging, in MR angiography and in susceptibility weighted imaging applications. Other fast imaging methods, such as parallel imaging and partial Fourier imaging also exist and can be used in conjunction with this approach. Every factor of two or four that can be accomplished can lead to better coverage and better resolution especially at high fields and in the brain where multi-channel coils lead to better and better signal-to-noise.

Conclusion

In summary, we have introduced a new iterative phase correction method that makes it possible to collect and correct for full two dimensional phase evolution in segmented EPI. The method is capable of removing chemical shift and geometric distortion. If this proves to be robust in clinical situations, then an extra time saving factor of two to four over and above that available with parallel imaging would have major implications for high resolution clinical applications of sequences such as susceptibility weighted imaging.

References

1. Mansfield P. Multi-planar image formation using NMR spin-echoes. J. Phys. C. 1977; 10: L5-L58.
2. Haacke, EM, Bearden FH, Clayton JR, Linga NR, Radiology, 1986; 158:521-529.
3. Feinberg, DA, Oshio Koichi, Phase errors in multi-shot echo planar imaging, Magn Reson Med 1994, 32:535-539.
4. Luk Pat GT, Meyer CH, Pauly JM, Nishimura DG, Reducing flow artifacts in echo-planar imaging, Magn Reson Med 1997, 37:436-447.
5. Beck G, Li D, Haacke EM, Noll TG, Schad LR, Reducing oblique flow effects in interleaved EPI with a center reordering technique, Magn Reson Med 2001, 45:623-629.
6. Haacke EM, Xu Y, Cheng YN, Reichenbach JR. Susceptibility weighted imaging. Magn Reson Med 2004;52612-8.
7. Weisskoff RM, Davis TL, Correcting gross distortion on echo planar images, Proceeding of the SMRM 11th Annual Meeting, Berlin, 1992. P 4515.
8. Jezzard P, Bababan RS, Correction for geometric distortion in echo planar images from B0 field variations, Magn Reson Med 1995, 34:65-73.
9. Reber PJ, Wong EC, Buxton KB, Frank LR, Correction of off-resonance related distortion in echo-planar imaging using EPI-based field maps, Magn Reson Med 1998, 39:328-330.

10. Liang Z-P, A model based method for phase unwrapping, IEEE Trans Med Imaging, 1996, 15:893-897.
11. Wan X, Gullberg GT, Parker DL, Zeng GL, Reduction of geometric and intensity distortions in echo-planar imaging using a multireference scan, Magn Reson Med 1997, 37:932-944.
12. Chen NK, Wyrwicz AM, Correction for EPI distortion using multi-echo gradient-echo imaging, Magn Reson Med 1999, 41:1206-1213.
13. Chen NK, Wyrwicz AM, Optimized Distortion correction technique for echo planar imaging, Magn Reson Med 2001, 45:525-528.
14. Schomberg H, Off-resonance correction of MR images, IEEE Trans. Med. Imag. 1999, vol. 18, 481-495.
15. Noll DC, Meyer CH, Pauly JM, Nishimura DG, Macovski A, A homogeneity correction method for magnetic resonance imaging with Time-varying gradients, IEEE Trans. Med. Imag. 1991, vol. 10, 629-637.
16. Pipe JG. Motion correction with PROPELLER MRI: application to head motion and free-breathing cardiac imaging. Mag. Reson. Med. 1999;42:963-969.

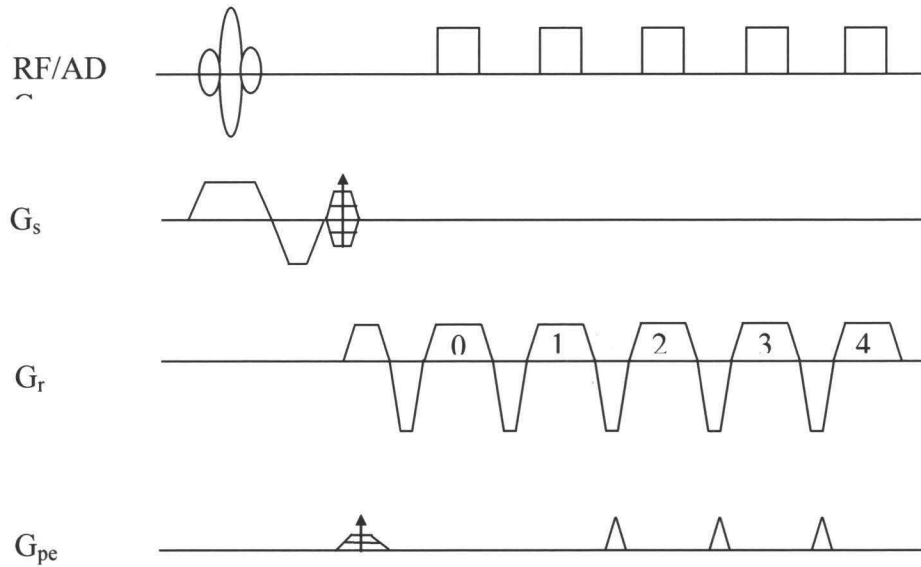


Figure 1. Sketch of the proposed sequence diagram with a TSF of 4. Only the even echoes in the echo train are sampled (this represents what is often referred to as a flyback method). The phase encoding gradient shown is for half of the k-space (for the other half, the polarity flips). Notice that there is no phase encoding between echo number 0 and 1.

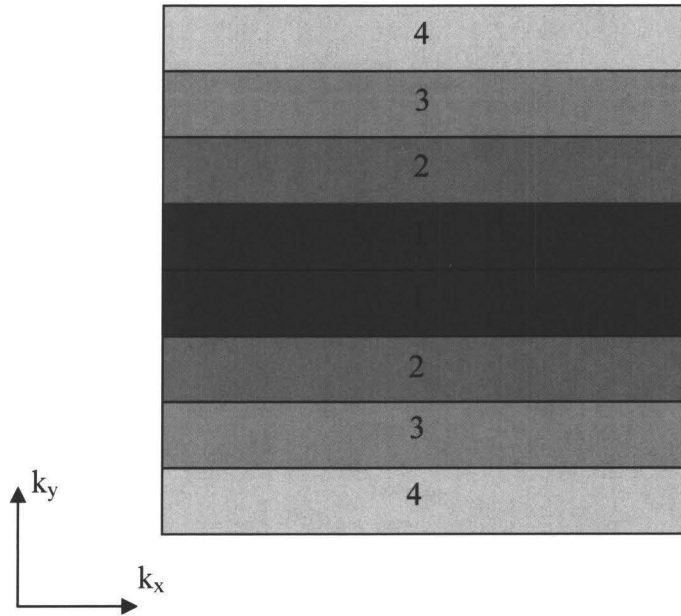


Figure 2. Sketch of the 2D k-space for a segmented EPI with a TSF of 4. Each shaded region is part of k-space acquired at the same echo time. The number in each shaded region corresponds to the echo number in the echo train (Fig. 1). Each region contains 32 phase encoding lines assuming the total number of lines in k-space is 256.

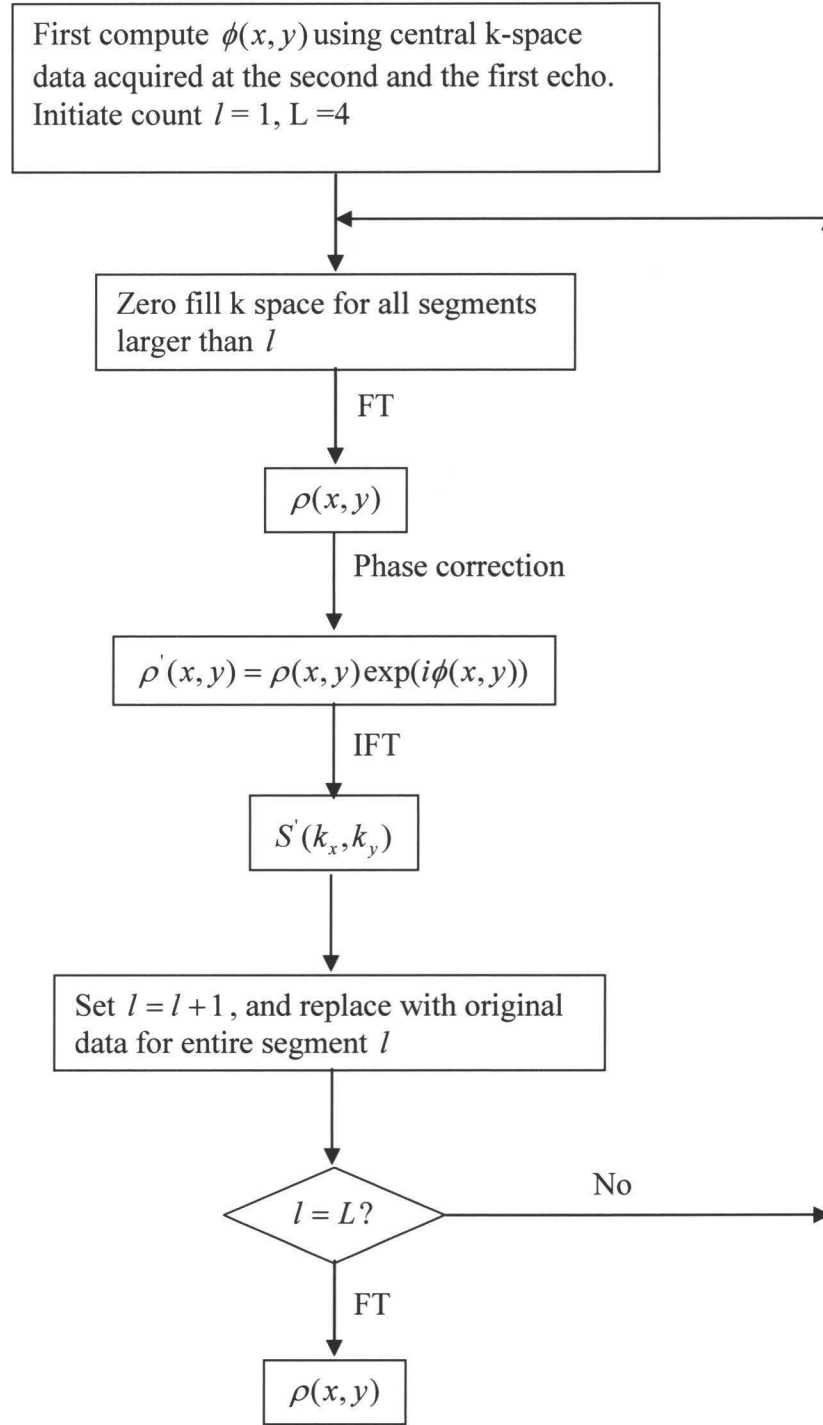


Figure 3. Schematic flow chart of the iterative reconstruction method.

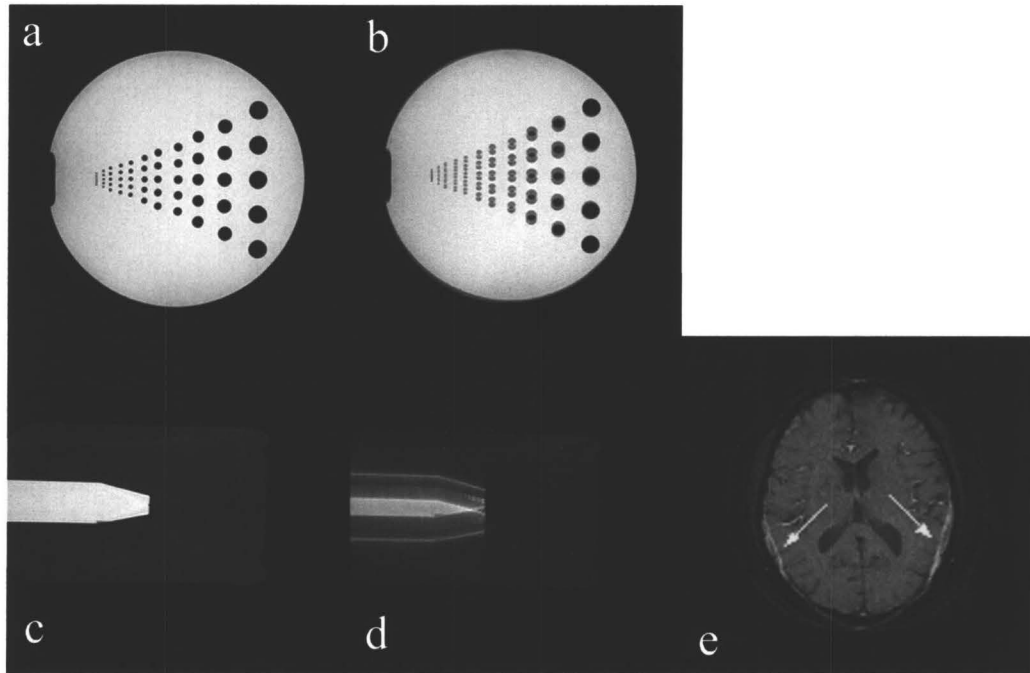


Figure 4. a) top left a gradient echo resolution phantom image as a reference. b) top right a simulated segmented EPI image with ETS and center out k-space trajectory. Note the duplication of the circles into two components. c) lower left a gradient echo oil/water phantom as a reference. d) lower middle a simulated segmented EPI image with ETS and center out k-space trajectory. Note the duplication of the oil into two components. e) lower right an in vivo brain image with ETS and center out k-space trajectory. Note the splitting of the fat into two components each shifting in opposite directions (yellow arrows on Fig. 4e)

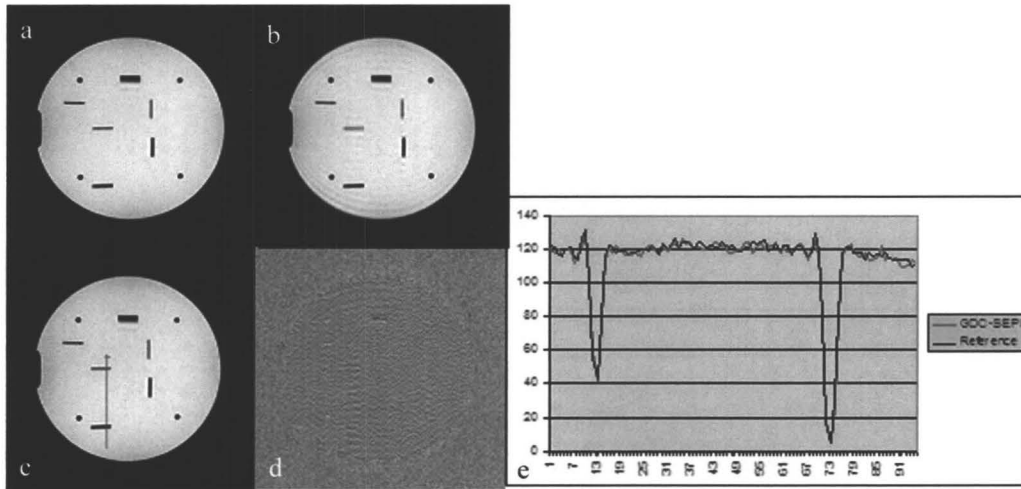


Figure 5. a) top left is a gradient echo image as a reference. b) top right is a simulated image without proposed iterative phase correction. c) lower left is the corrected GDC-SEPI image. d) lower middle is the residual image between a) and c). e) lower right shows the measured profiles across the pixels along the red line on d). Note: the red line is across the visible coherent ringings between two resolution bars, which also happens to be close to the highest residual error. The measured profiles indicate that the biggest residual is still within the noise level.

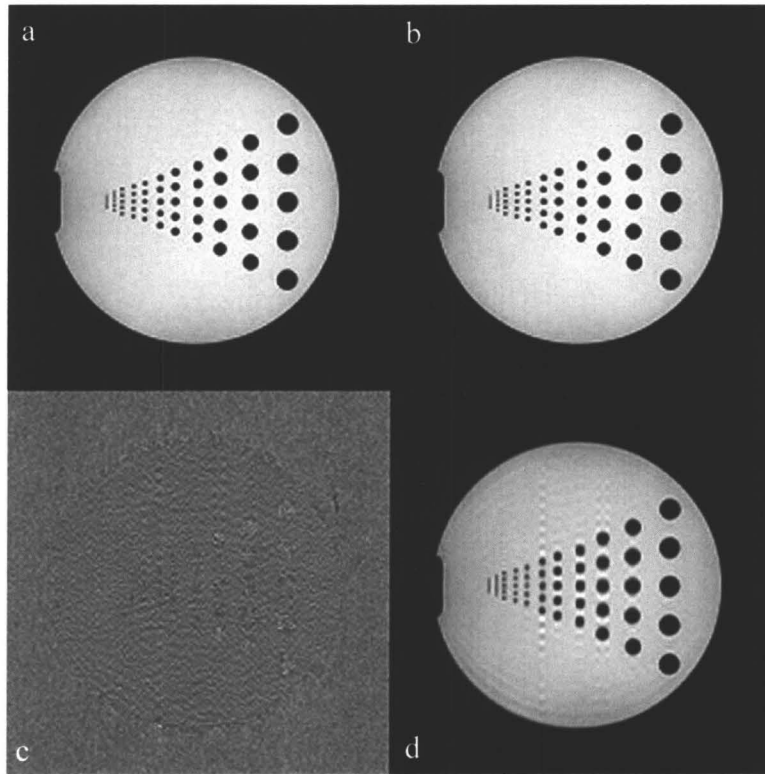


Figure 6. a) top left is a reference gradient echo image. b) top right is a GDC-SEPI image after phase correction. c) lower left is the residual image between a) and b). d) lower right is image b) before phase correction. Note the dramatically reduced coherent ringing after phase correction.

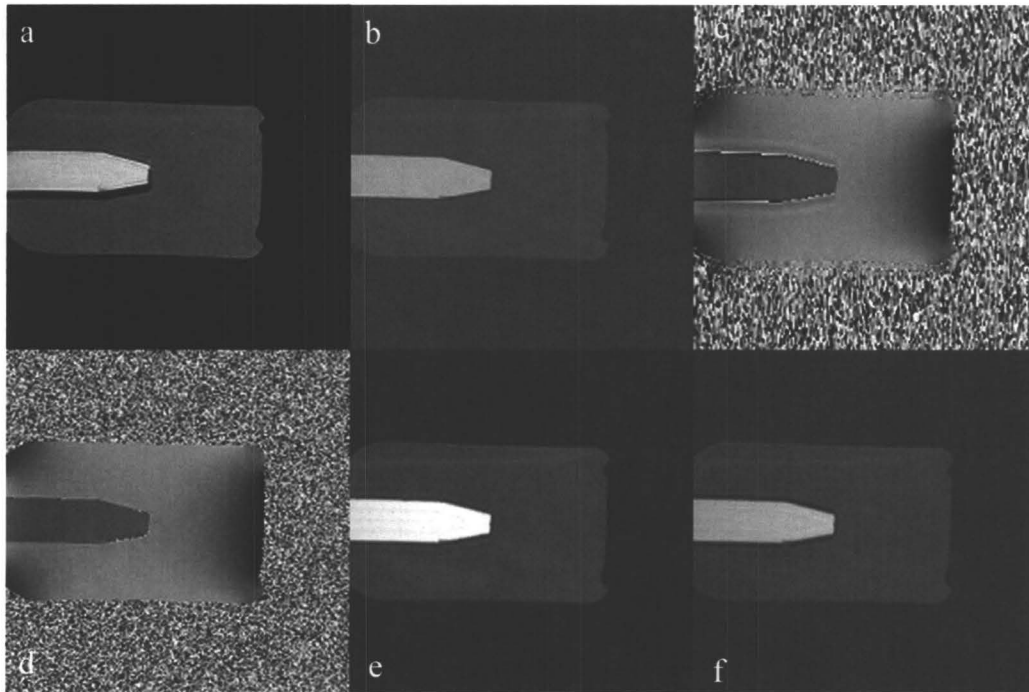


Figure 7. a) top left a SEPI image. b) top middle a gradient echo image. c) top right a phase image from central k-space. d) lower left a phase image from all of k-space. e) lower middle a GDC-SEPI image using d) as a phase map. f) lower right a GDC-SEPI image using c) as a phase map.

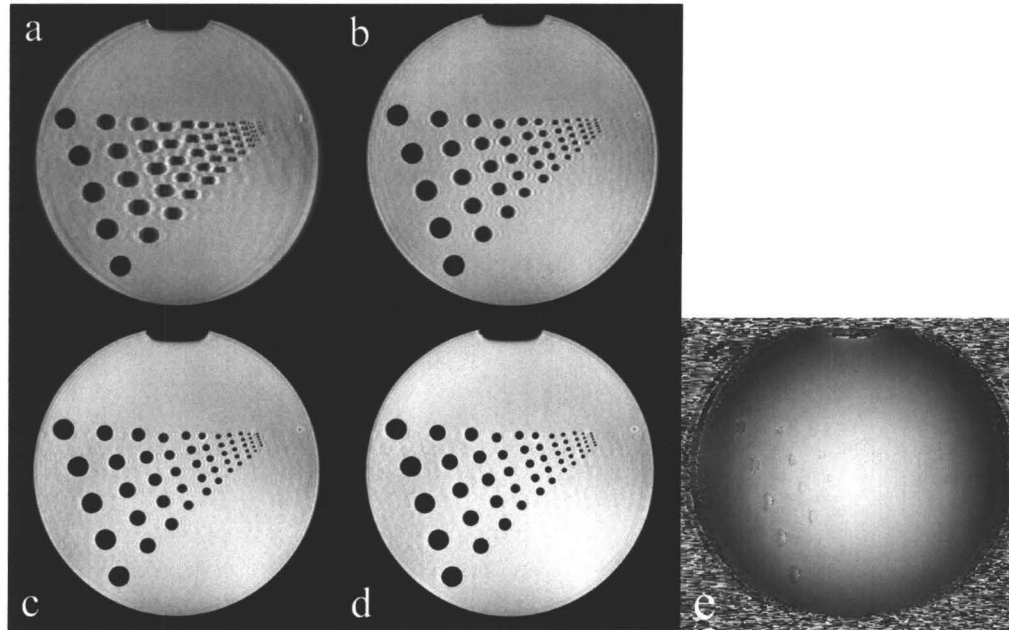


Figure 8. a) magnitude image reconstructed without the proposed iterative phase correction; b) magnitude image reconstructed after the first iteration; c) magnitude image reconstructed after the second iteration; d) magnitude image reconstructed after the final (third) iteration of the phase correction. e) lower right the phase map estimated from the central k-space.

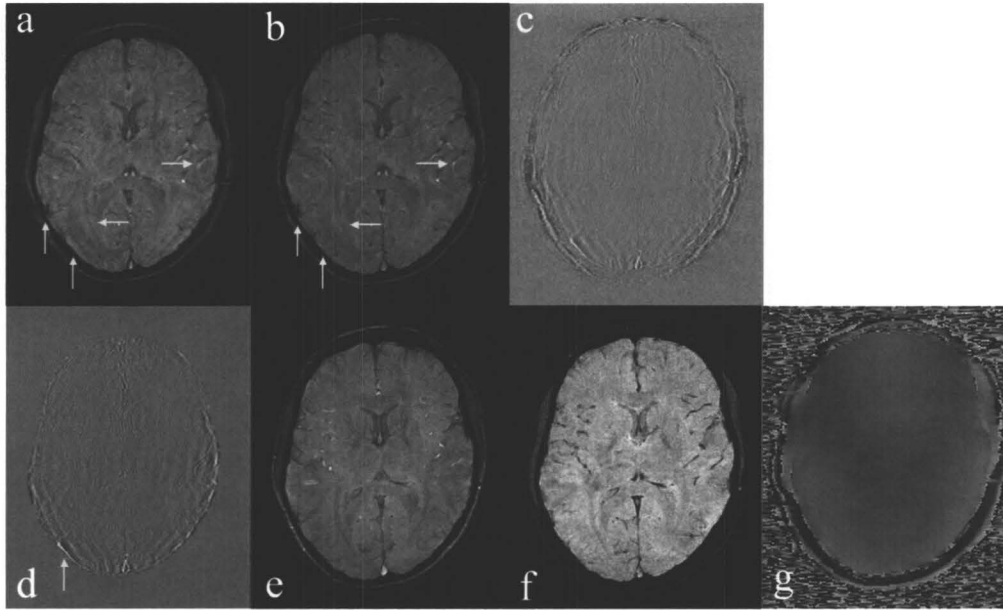


Figure 9a) magnitude image of a human brain before proposed phase correction; 9b) magnitude image reconstructed after the proposed phase correction; 9c) residual image between 9a and 9b); 9d) same as 9c) except only showing the signal change in the area of brain parenchyma; 9e) magnitude image acquired with a conventional SWI sequence; 9f) magnitude image acquired with a sequential sampled SEPI sequence. 9g) lower left, phase map estimated from the central k-space. Note: the sharpened vessel and optic radiation (horizontal arrows on 9a and 9b). The vertical arrows point to the much improved magnitude image.

Chapter 5

Conclusions and Future Directions

Conclusions

Susceptibility Weighted Imaging utilizes the susceptibility difference between tissues to create a new imaging contrast in MRI other than proton density, T1-, or T2-weighted imaging. SWI is an extension of conventional T2*-weighted gradient echo imaging. However, optimizing the SWI acquisition scheme also takes into account signal cancellation effects and post processing to enhance the magnitude contrast by using added information in the phase image. In addition, phase images can provide excellent contrast between gray matter, white matter, iron-laden tissues, venous blood vessels and other tissues with susceptibilities that are different from the background.

The problem with phase images has generally been the presence of global background fields that confound the effects of local phase changes in tissue. However, when global background fields and susceptibility changes between local tissues have distinct spatial frequencies, we can use a high-pass filter to remove unwanted global effects. For large objects of interest such as the putamen, the high-pass filtering approach may lose phase contrast after filtering; this is one of the major weaknesses of the method. In general, the larger the object, the less

effective the high-pass filtering. At high field, phase aliasing is another problem that has to be addressed before performing high-pass filtering. At the boundary of air/tissue interface, rapid variation of phase creates spurious high spatial frequency that makes high-pass filtering ineffective. However, if we can attain a pristine phase image with background field changes removed, it is possible to differentiate one type of tissue from another in the magnitude image with the contrast presented in the phase image thanks to the different local susceptibilities of the tissues.

The post processing using magnitude and phase filtered images to create an SWI image involves the following steps: 1) high-pass filtering the phase image; 2) creating a phase mask from the phase image using a ramp-like function ranging from zero to unity; 3) multiplying the phase mask into the magnitude image a certain number of times; and 4) performing minimum intensity projection over a few adjacent slices. In Chapter 2, the mathematical formula of how CNR between tissues with different susceptibility varies with phase (and hence echo time) and the number of times the phase mask multiplication is presented. The number of phase mask multiplication is chosen to optimize the CNR of the SWI image and generally depends on the phase jump inside the object of interest.

We consider first tissues which have the same signal with Gaussian noise, and contrast is generated only by the phase images. The contrast in the magnitude

image is initially zero and contrast appears only after the multiplication of phase mask. The phase is proportional to the echo time at which the image is acquired and it must be remembered that the MR signal decays according to $\exp(-TE/T2^*)$. One more factor to take into account is the imaging time (since the initial SNR is proportional to the square root of total imaging time). So practically we are forced into a constant time imaging constraint. We find that there is a point where it's better to run the scan twice and average the data with half of the echo time than to run the scan one time with a long echo time to increase the phase difference between tissues. A long echo time also creates a phase aliasing problem, which could make the phase mask multiplication ineffective or create unwanted artifacts such as a broadening of the apparent vessel size. In this sense, a relatively lower phase difference is preferred. For constant imaging time, a lower phase value (shorter echo time) with more averages yields a higher contrast or higher visibility. The number of multiplications needed for a phase of 0.3π or greater is 4 or less. For a phase of 0.3π or less one should use 4 or more multiplications. The noise is increased in the SWI image as the number of the phase mask multiplications increases. The best value of the number of the multiplications is the smallest one that meets the desired CNR. This is particularly true if the minimum intensity projection (mIP) is to be performed afterwards (the more noise is present, the worse the mIP will be). As far as veins are concerned, there will be a spread of phases partly because of partial volume effects and partly because of the angles at which veins are positioned to the main field. We have concluded that

roughly 4 times phase mask multiplication yields either optimal or close to optimal CNR.

In Chapter 2, all the discussion revolves around a simplified one compartment model. To better understand how phase changes with the echo time for small veins, we will have to take into account partial volume effects, the topic presented in Chapter 3. For venous vessels that are parallel to the main magnetic field, the biggest signal cancellation occurs when the venous vessel is out of phase relative to the brain parenchyma in the same voxel. This translates to an echo time of about 50 ms at 1.5T. For the venous vessels that are perpendicular to the main magnetic field, the apparent phase of a voxel turns out to be resolution or aspect ratio dependent. Understanding how phase varies with image orientation and vessel aspect ratio helps to guide us how to optimize SWI acquisition. In Chapter 3, apparent voxel phase is simulated relative to the voxel aspect ratio for the venous vessel perpendicular to the main magnetic field. The simulation tries to answer: 1) Why is the apparent phase of a voxel negative for the scan in the transverse orientation while the phase is positive for the scan in the sagittal orientation? Different phase behavior requires a different phase mask to do the post processing. 2) How does the apparent phase of a voxel which contains the venous vessel change as a function of resolution, echo time, and relative volume ratio of venous blood with the background tissue? 3) What is the phase profile for

the voxels adjacent to the voxel which contains the vessel? The profile may reveal any vessel broadening due to the phase mask multiplication.

Here is the brief summary of the findings to those questions. From an analytical point of view when there is no partial volume effect, the phase itself for the venous vessel perpendicular to the main magnetic field is positive while the phase outside the vein is modulated by the $\cos 2\phi$ term. For a transverse acquisition when the slice thickness is larger than the in-plane voxel size, the net integration of the complex signal over the voxel yields negative phase. This is because the thick slice basically integrates along a narrow region directly above the vessel where the angle ϕ is close to zero. This long thin voxel is then dominated by a negative phase outside the vessel while the adjacent voxel has net positive phase. On the other hand, a conventional sagittal acquisition simply results in a positive phase because both the phase for the vessel itself is positive and the region outside the vessel is dominated by the positive phase as well. It's fairly straightforward to conclude that the partial volume effect implies that the apparent phase of a voxel depends on the imaging resolution and aspect ratio. The simulation shows that the highest negative phase is seen for the transverse acquisition when the slice thickness is about 4 times the in-plane voxel dimension. This translates to 0.5 mm in-plane resolution for a usual 2 mm slice thickness. However, it's quite obvious that the volume fraction of the vessel to the voxel size directly affects the net apparent phase of the voxel. With a fixed 1:4 in-

plane to slice thickness ratio, the smaller the volume fraction, the smaller the net negative phase (in an absolute sense). With a small volume fraction, the apparent voxel phase is close to being a linear function of the echo time but with a small slope. With a large volume fraction, at long echo times the apparent voxel phase is no longer linear with echo time. At long echo time, aliasing could be a potential problem for an image containing vessels of various sizes. These observations indicate that higher resolution is needed to see smaller veins. To image a certain size of vessel, the simulated result gives a guideline about what resolution and which echo time are needed. It's worth noting that at TE of 15ms at 4T which is equivalent to TE of 40ms at 1.5T, the apparent voxel phase is about 0.1π for a vessel of 500 microns in diameter at $0.5 \times 0.5 \times 2.0 \text{ mm}^3$ resolution. For smaller size vessels, the apparent voxel phase is smaller than 0.1π . The simulated in-plane phase profiles perpendicular to the vessel show that the phase one pixel away is positive compared with the negative phase of the pixel containing the vessel, which implies that there is no vessel broadening (in-plane) if the negative phase mask is applied. Although the resolution of $0.5 \times 0.5 \times 1.0 \text{ mm}^3$ gives the highest signal cancellation effect, the resolution of $0.5 \times 0.5 \times 2.0 \text{ mm}^3$ gives equivalent CNR after phase mask multiplication. If we keep the same imaging time for both resolutions, then the resolution of $0.5 \times 0.5 \times 2.0 \text{ mm}^3$ will have higher CNR after phase mask multiplication. The simulated through-plane phase profiles perpendicular to the vessel also in favor of the resolution of $0.5 \times 0.5 \times 2.0 \text{ mm}^3$ to have less broadening artifact in through-plane direction. It has less effect on

mIPped images. However, if the total volume of vessels is the main interest of the study then vessel broadening along the through-plane direction can inflate the number. For the resolution of $0.5 \times 0.5 \times 2.0 \text{ mm}^3$, there is only a 10% enhancement of CNR after the phase mask multiplication. With relatively low SNR at high resolution, a 10% change of CNR might not be significant.

In summary, the simulated phase behavior answers why the transverse acquisition is perhaps the best way to collect susceptibility weighted imaging data when the main field is along the long axis of the body. While the apparent voxel phase is a function of voxel aspect ratio, the simulation predicts that the best aspect ratio to use for SWI imaging is $R:w:h = 1:1:4$ (where R is the diameter of the vessel of interest, w is the in-plane resolution and h is the slice thickness). There is no in-plane vessel broadening after the phase mask multiplication. With $R:w:h = 1:1:4$ the through-plane vessel broadening is not significant.

In the simulation, we model the vessel as an infinitely long cylinder perpendicular to the main magnetic field. It is a simplified model. However, assessment of experimental observations confirm it to be effective (Fig. 7 and Fig. 9 in Ch. 3). Eq. [2] and Eq. [3] give the dependence of both intra-vascular field and the extra-vascular field to the angle ϑ of a vessel to the main field. Both $\cos^2 \vartheta$ dependence for intra-vascular field (Eq. [2]) and $\sin^2 \vartheta$ for extra-vascular field (Eq. [3]) make the result insensitive to slight deviations from perpendicular

orientations to the main field (the majority of veins we observe in the transverse orientation appear to be nearly perpendicular to the main field especially for those lateral cervical veins). A larger deviation reduces both intra-vascular and extra-vascular fields. Collecting the data in a transverse orientation with higher slice thickness relative to in-plane resolution still yields negative phase. For certain angles the phase inside the vessel may turn negative, which results in net negative phase because areas both inside and outside the vessel are now with negative phase. In conclusion, a transverse orientation is the best choice for SWI acquisitions because it results in consistent negative phase behavior.

For Susceptibility Weighted Imaging, long echo times coupled with high resolution translates to a long acquisition time. In Chapter 4, we look into gradient echo segmented EPI (SEPI) as an alternative approach to conventional SWI sequence (which is a 3D fully velocity compensated gradient echo sequence). SEPI has the advantage of speeding up acquisition. However, issues like ghosting, geometric distortion, and flow related misregistration associated with SEPI have to be addressed before applied to SWI. One specific feature about SWI is its natural separation of arterial signal (bright) from the venous signal (dark). Conventional SEPI makes both arterial and venous signals dark. We modified the conventional SEPI sequence to a Geometric Distortion Corrected SEPI (GDC-SEPI) sequence to address issues related to the conventional SEPI approach. First, we utilize a center out k-space trajectory instead of the routine bottom up k-space

trajectory. With a fly-back structure on readout echo train, the flow is compensated along that direction to make the arterial signal bright again. Simulation shows that the routine echo time shift (ETS) technique is not suitable to a center out k-space trajectory. With a center out k-space trajectory, ETS doubles the geometric distortion as well as adds additional distortion in opposite direction. To correct the discontinuities between k-space data from different echoes, one additional echo is added to the front of the readout echo train but without phase encoding between the additional echo and the original readout echo train. The k-space data acquired at the additional echo added samples the same central k-space as the data acquired on the first echo of the original echo train. This ensures that we can use those two datasets to estimate the phase evolution between echoes. With the estimated phase map, an iterative correction is then carried out to remove the phase discontinuities between data from different echoes. The iterative correction method is fast in terms of computation compared with a brute force approach which requires a full 2D Fourier transform for each pixel. For a modest speed up, four segments, the whole iterative correction only needs 2D Fourier transforms.

The simulated phantom results indicate that under smooth field variation assumption, this method works very well. However, images from real acquisition of the same phantom show some residual artifacts more significant than that on the images from the simulation. The reason for this could be the phase estimated

from real acquisition is not as perfect as in the case of simulation. For example, phase changes from the eddy currents are not accounted for in the estimated phase map. To improve the accuracy of the phase estimate is one of the future directions to bring this method to the clinical environment.

With rapid field change like at the boundary of fat/water, this method could suffer. However, the simulated fat signal doesn't show the usual shift as expected with the conventional SEPI sequence. That itself shows that GDC-SEPI does correct geometric distortion. To have a better phase estimate at the areas of rapid phase change, one way is to reduce the speed up factor (or segments). The other is to increase the resolution hence with the same speed up factor, the central k-space used for estimating the field change is bigger. *In vivo* data shows a promising future for the GDC-SEPI method. Though the overall improvement of *in vivo* images may not be as evident as in the phantom which has very sharp edges, the iterative correction has still made a significant improvement to sharpen the image and to reduce artifacts.

Future Directions

The GDC-SEPI method uses iterative phase correction to remove chemical shift and geometric distortion associated with SEPI. Phantom and *in vivo* data show a promising future. However, the method has to be tested to be robust in a clinical environment. The estimate of phase evolution between echoes is the key to the

success of the method. Careful mapping of phase contributions from sources such as eddy current has to be done. Parallel imaging is available for most systems today. High speed up factors with parallel imaging can degrade SNR too much. However, combining GDC-SEPI with a moderate speedup factor with parallel imaging could further reduce the acquisition time without a big hit on SNR. This is one of the interesting areas to work on in the future.

Susceptibility Weighted Imaging has proved to be an important tool for studying a variety of neurovascular disorders like trauma, brain tumor, stroke and aging. Quantitative estimation of magnetic susceptibility (or susceptibility mapping) of tissue from the phase images is the way to take SWI to next level. To get pristine phase maps with only phase variations from local substructures from the SWI phase images requires removal of the aliasing seen throughout the phase image. High-pass filtering only works well to remove slow varying background field. The tough challenge is to get rid of rapid phase variation seen at the boundary of air/tissue interface. There are a few approaches to the problem. One approach is to do high-pass filtering after phase unwrapping. Rapid phase variation at the air/tissue boundary creates spurious high frequency spatial change, which means heavy high-pass filtering might be needed. That reduces the phase contrast for the substructures in interest. Another approach is to do polynomial fitting of baseline phase changes after phase unwrapping and then subtracted the baseline from the unwrapped phase image to leave the phase

change from the substructures. The problem is a global fitting for the whole image is not an easy task. One might have to do fitting region by region and then combine the results together. Another interesting approach is forward modeling the field affects of the air/tissue pockets using a priori information of the geometries of those air/tissue pockets and then subtract the simulated field affects from the original phase image [25-26]. Overall, this remains an exciting area of research that has the potential to help better diagnose patients and image the vasculature of the brain. If the above approaches are successful, SWI will be used more and more clinically.

Bibliography

1. Beck G, Li D, Haacke EM, Noll TG, Schad LR, Reducing oblique flow effects in interleaved EPI with a center reordering technique, *MRM*, 2001; 45: 623-629.
2. Constable RT, Functional MR gradient-echo imaging using Echo Planar Imaging in the presence of large inhomogeneities, *JMRI*, 1995; 5:746-752.
3. Conturo TE, Barker PB, Mathews V, Monsein LH, Bryan N, MR Imaging of cerebral perfusion by phase-angle reconstruction of bolus paramagnetic-induced frequency shifts, *MRM*, 1992; 27: 375-390.
4. Crespigny AJ, Roberts T, Kucharczyk J, Moseley ME, Improved sensitivity to magnetic susceptibility contrast, *MRM*, 1993; 30:135-137.
5. Feinberg, DA, Oshio K, Phase errors in multi-shot echo planar imaging, *MRM*, 1994, 32:535-539.
6. Griswold MA, Jakob PM, Heidemann RM, Nittka M, Jellus M, Wang J, Kiefer B, Haase H, Generalized autocalibrating partially parallel acquisitions (GRAPPA), *MRM*, 2002; 47:1202-1210.
7. Haacke EM, Brown RW, Thompson MR, Venkatesan R. Magnetic resonance imaging, physical principals and sequence design. New York: Wiley-Liss; 1999. p746-757.
8. Haacke EM, Lai S, Dmitriy A. Yablonskiy, Weili Lin, In vivo validation of the bold mechanism: A review of signal changes in gradient echo

- functional MRI in the presence of flow, *International Journal of Imaging Systems and Technology*, 1995; 6:153-163.
9. Haacke EM, Xu Y., Cheng YN, Reichenbach JR, Susceptibility weighted imaging (SWI). *MRM*, 2004; 52: 612-618.
 10. Haacke EM, Sehgal V, DelProposto Z, Chaturvedi S, Imaging Cerebral Amyloid Angiopathy with Susceptibility Weighted Imaging: A Case Report. *AJNR* 2007. 28(2): p. 316-7.
 11. Haacke EM, Khan A, Manova ES, Krishnamurthy B, Gollapalli L, Ciulla C, Kim I, Petersen F, Kirsch W., Establishing a baseline phase behavior in magnetic resonance imaging to determine normal vs. abnormal iron content in the brain. *JMRI*, 2007; 26:256-64.
 12. Haacke EM, Yu Y, Kido D, Observing Tumor Vascularity Noninvasively Using Magnetic Resonance Imaging. *Image Anal Stereol* 2002; 21:107-113.
 13. Hinshaw W.S, Lent A.H, An introduction to NMR imaging: from the Bloch equation to the imaging equation. *Proc. IEEE*, 1983; 71: 338.
 14. Jezzard P, Bababan RS, Correction for geometric distortion in echo planar images from B0 field variations, *MRM*, 1995; 34:65-73.
 15. Juhasz C, Hu J, Venous Collaterals in Sturge-Weber Syndrome: Relations to Cortical Metabolism, White Matter Integrity and Neuro-cognitive Functions. *AJNR*, 2007. 28(5): p. 900-6.

16. Klarho M, Dilharreguy B, Gelderen PV, Moonen CTW, A PRESTO-SENSE sequence with alternating partial Fourier encoding for rapid susceptibility-weighted 3D MRI time series, *MRM*, 2003; 50:830-838.
17. Lai S, Reichenbach JR, Haacke EM. Commutator filter: a novel technique for the identification of structures producing significant susceptibility inhomogeneities and its application to functional MRI. *MRM*, 1996; 36:781-787.
18. Lamba M, Holland SK, Schmithorst V, Dardzinski B, Francesco d'Errico, Nath R, Fast high-resolution 3D segmented echo planar imaging for dose mapping using a superheated emulsion chamber, *MRM*, 2003; 49: 675-681.
19. Lauterbur P.C, Image formation by induced local interactions: Examples employing NMR. *Nature*, 1973, 242: 190.
20. Lee JH, Hargreaves BA, Hu BS, Nishimura DG, Fast 3D imaging using variable-density spiral trajectories with applications to limb perfusion, *MRM*, 2003; 50:1276-1285.
21. Linfante I, Llinas RH, Caplan LR, Warach S, MRI features of intracerebral hemorrhage within 2 hours from symptom onset. *Stroke*, 1999; 30:2263-2267.
22. Liu G, Sobering G, Duyn J, Moonen CTW, A functional MRI technique combining principles of echo-shifting with a train of observations (PRESTO), *MRM*, 1993; 30:764-768.

23. Meyer CH, Hu BS, Nishimura DG, Macovski A, Fast spiral coronary artery imaging, *MRM*, 1992; 28:202-213.
24. Moonen CTW, Liu G, Gelderen PV, Sobering G, A fast gradient-recalled MRI technique with increased sensitivity to dynamic susceptibility effects, *MRM*, 1992; 26: 184-189.
25. Neelavalli J, Cheng NY, Haacke EM, Improved Fourier Based Method for Calculating Field Inhomogeneity from Known Susceptibility Distribution. *Proceedings of the 15th Annual Meeting of ISMRM*, 2007: p. 1016.
26. Neelavalli J, Cheng NY, Haacke EM, Method for Susceptibility Calculation in Multiple Source Object Distribution with Arbitrary Susceptibilities: A Preliminary Report. *Proceedings of the 13th Annual Meeting of ISMRM*, 2005.
27. Ogawa S, Lee TM, Kay AR, Tank DW. Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proc Natl Acad Sci USA* 1990; 87: 9868-9872.
28. Ogawa S, Lee TM. Magnetic resonance imaging of blood vessels at high fields: in vivo and in vitro measurements and image simulation. *MRM*, 1990; 16: 9-18.
29. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *MRM*, 1990; 14: 68-78.

30. Parikh A.M, Magnetic Resonance Imaging techniques. Elsevier, New York, 1992.
31. Pruessmann KP, Weiger M, Scheidegger MB, and Boesiger P, SENSE: Sensitivity Encoding for Fast MRI, MRM, 1999; 42:952-962.
32. Reichenbach JR, Haacke EM, High-resolution BOLD venographic imaging: a window into brain function, NMR Biomed, 2001; 14:453-467.
33. Reichenbach JR, Ramesh Venkatesan, Dmitriy A. Yablonskiy, Michael R. Thompson, Song Lai, E. Mark Haacke, Theory and application of static field inhomogeneity effects in gradient-echo imaging, JMRI 1997; 7: 266-279.
34. Reichenbach JR, Venkatesan R, Schillinger DJ, Kido DK, Haacke EM. Small vessels in the human brain: MR venography with deoxyhemoglobin as an intrinsic contrast agent. Radiology 1997;204:272–277.
35. Reichenbach JR, Essig M, Haacke EM, Lee BC, Przetak C, Kaiser WA, Schad LR. High resolution venography of the brain using magnetic resonance imaging. MAGMA 1998; 6:62–69.
36. Rosen BR, Belliveau JW, Vevea JM, Brady TJ, Perfusion imaging with NMR contrast agents, MRM, 1990; 14:249-265.
37. Sehgal V, Haddar D, Haacke EM, Sloan AE, Zamorano LJ, Barger G, Hu J, Xu Y, Prabhakaran KP, Elangovan IR, Neelavalli J, Reichenbach JR, Susceptibility-weighted imaging to visualize blood products and improve tumor contrast in the study of brain masses. JMRI, 2006; 24:41-51.

38. Sehgal V, Zachary D, Haacke EM, Tong K, Wycliffe N, Kido D, Xu Y, Neelavalli J, Haddar D, Reichenbach JR, Clinical applications of neuroimaging with susceptibility-weighted imaging, JMRI, 2005; 22: 439-450.
39. Sodickson DK, Manning WJ, Simultaneous acquisition of spatial harmonics (SMASH): Fast imaging with radiofrequency coil arrays, MRM, 1997; 38:591-603.
40. Stark D.D and Bradley W.G, Magnetic Resonance Imaging, St. Louis, Mo.: C.V. Mosby, 1988.
41. Thulborn KR, Waterton JC, Matthews PM, Radda GK, Oxygenation dependence of the transverse relaxation time of water protons in whole blood at high field, Biochim Biophys Acta, 1982; 714:265-270.
42. Tong KA, Holshouser BA, *Axonal Injury in Children: Clinical Correlation with Hemorrhagic Lesions*. . Ann Neurol , 2004; 56:36-50.
43. Vadim Y U. Kuperman, Jonathan N. River, Martha Z. Lewis, Leslie M. Lubich, Gregory S. Karczmar, Changes in T2*-Weighted Images During Hyperoxia Differentiate Tumors from Normal Tissue, MRM, 1995; 33: 318-325.
44. Vlaardingerbroek M.T, Boer J.A den, Magnetic Resonance Imaging: Theory and Practice. Springer-Verlag, Berlin, 1996.

45. Wang Y, Yu Y, Li D, Bae KT, Brown JJ, Lin W, Haacke EM. Artery and vein separation using susceptibility-dependent phase in contrast-enhanced MRA. *JMRI*, 2000; 12:661–670.
46. Weiskoff RM, Kiihne S. MRI susceptometry: image-based measurement of absolute susceptibility of MR contrast agents and human blood. *MRM*, 1992; 24:375.
47. Wycliffe D, Holshouser BA, Oyoyo UE, Haacke EM, Kido DK. , Reliability in detection of hemorrhage in acute stroke by a new three-dimensional gradient recalled echo susceptibility-weighted imaging technique compared to computed tomography: a retrospective study. *JMRI*, 2004; 20:372-377.
48. Xu Y, Haacke EM, Partial Fourier Imaging in multi-dimensions: a means to save a full factor of two in time, *JMRI*, 2001; 14:628-635.
49. Xu Y. and Haacke EM, The role of voxel aspect ratio in determining apparent vascular phase behavior in Susceptibility Weighted Imaging, *MRI*, 2006; 24:155-160.
50. Yablonskiy DA, Haacke EM. Theory of NMR signal behavior in magnetically inhomogeneous tissues: the static dephasing regime. *MRM*, 1994; 32: 749-763.