Susceptibility
Weighted Imaging in MRI
Susceptibility Weighted Imaging in MRI
Basic Concepts and Clinical Applications

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Since its inception, magnetic resonance imaging has used tissue properties such as $T_1$, $T_2$, and spin density followed by flow, diffusion characteristics, lipid imaging, and spectroscopy as the technology developed to create images with extraordinary detail of the body and brain; and this list continues to grow. Surprisingly, prior to susceptibility weighted imaging or SWI, the basic property of tissue susceptibility had not been used directly, but rather taken advantage of through local $T_2^*$ effects in magnitude images. The problem with this approach is that many different sources can cause $T_2^*$ signal dephasing. The basic field effects created by susceptibility have generally been recognized as a source of artifacts and the usual first response was to remove them. However, such field effects can be used to separate types of materials such as calcium deposits, which are diamagnetic, from microbleeds, which are paramagnetic. In fact, these field effects were used in the original concept of susceptibility weighted imaging to better image small veins and to enhance contrast in tissues.

Practically, the phase information available in MR imaging carries all the information that is needed to reconstruct the local magnetic source or susceptibility difference between tissues. Although SWI uses phase as a source of contrast, the more advanced concept is to create a susceptibility map that can be used not only to differentiate paramagnetic from diamagnetic substances but also to quantify the amount of a given substance present that is causing the susceptibility difference, such as local iron differences between tissues. In this book, we refer to the combination of SWI filtered phase and magnetic susceptibility mapping as SWIM for susceptibility weighted imaging and mapping. The work on SWI showed the significance of phase in enhancing contrast in tissues and now SWIM opens the door to quantifying susceptibility in tissues. Clinically, SWI makes it possible to image microbleeds and veins more effectively, while SWIM will provide the methods to quantify oxygen saturation and local iron content. These techniques have or will find applications in neurovascular diseases, neurodegenerative diseases, and iron-related diseases. Multi-echo SWI also offers a means to image the
entire vascular system, including arteries and veins alike. The field is still developing, and there are hints that major roadblocks in this area are falling, thanks to technical advances in magnet homogeneity, gradient strengths, and faster imaging methods such as parallel imaging. For example, the need to accommodate or correct air/tissue interfaces is now theoretically possible, high bandwidth imaging avoids geometric distortion, and multi-echo imaging may offer a means to ideally phase unwrap data on a pixel by pixel basis. This book contains nearly every aspect of SWI; however, a number of new developments and new findings are being made at the time this book went into publication. As these new concepts in the field of MRI evolve and develop, some of them may be ready for incorporation into the next edition of the book.

The main aim of this book is to provide clinicians a detailed overview of the basic concepts and applications related to susceptibility weighted imaging. The book has been organized into three parts. In the first eight chapters, we introduce basic concepts that include the definitions and mechanisms of gradient echo imaging, phase, $T_2^*$, and multi-echo imaging. This will enable the reader to have an understanding of the basics of the terms used throughout the book. The next 12 chapters represent the current efforts in clinical translational research using SWI. These chapters cover the basic venous structures in the brain followed by the application of SWI in several diseases, such as cancer, traumatic brain injury, vascular dementia, stroke, hemorrhage, multiple sclerosis, venous malformations, Sturge–Weber syndrome, atherosclerosis, and calcifications in breast cancer. The final 16 chapters cover a variety of technically more advanced concepts, including susceptibility mapping (SWIM), oxygen saturation measurements, technical developments, and animal imaging, as well as a list of references related to SWI up to early 2010. Most of the images used in this book have been adapted from published journal articles. Since most of these were either from Journal of Magnetic Resonance Imaging (JMRI) or Magnetic Resonance in Medicine (MRM), both published by John Wiley & Sons Inc., a blanket permission was acquired for their use in this book. Acknowledgement for the figures adapted from other publications are specifically mentioned in their respective captions.

The increasing clinical applications of SWI were our inspirations to write and produce this book. We believe its recent growth into SWIM and susceptibility mapping will spearhead even more quantitative measures of iron and new applications ranging from neurodegenerative diseases to hemochromatosis. Many colleagues around the world have made efforts in developing clinical applications of SWI and many, if not most of them, have contributed to this book. We acknowledge the contributions of these experts in the field. Without their enthusiasm and continuous support, including numerous meetings at various conferences, this project would not have been possible.

We are indebted to all those people who helped us in bringing out this book, particularly Alexander Boikov, Daniel Haacke, Lisa Hamm, and Judith Farah. Yongquan Ye helped us with his technical expertise in refining several chapters. A very special thanks to Jaladhar Neelavalli for his careful reading of the book, for his meticulous attention to detail, and for coordinating the final efforts that made it possible to get this book to press, in a timely fashion. We acknowledge Wiley for taking on this project and for their expert professional editorial support, particularly that of Dean Gonzalez, Kristen Parrish, and Ms. Sanchari Sil. We are grateful to Thom Moore, editor at Wiley, for his patience and enthusiasm in bringing out this book. A special thanks is due to the people at Siemens Healthcare for having made SWI available as a product for their customers. This was a major
step in taking the methodology into the clinical domain and, in part, is the reason why so many new applications are developing for SWI now. Finally, we would like to thank our families who put up with the added responsibilities during our long hours of work. Their emotional support and patience made this book possible.

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Part I

Basic Concepts
Susceptibility weighted imaging (SWI) in its current form has only recently entered the realm of magnetic resonance imaging (MRI) techniques despite the fact that magnetic susceptibility, $\chi$, is certainly of central importance in the field of magnetism and magnetic resonance. SWI is an MRI method that takes advantage of signal loss and phase information to reveal important anatomical and physiological information about vessels and tissues. To date, it has been used predominantly in the brain, but is now beginning to find uses in other parts of the body as well. All current applications will be addressed in this book. With the clinical use of SWI now in place at hundreds of sites around the world, it is likely that radiologists and researchers alike will continue to discover new applications throughout the body.

Although being relatively young in age, the method already has some history and has changed its name from its infancy to later developments. Originally, it was referred to as high-resolution BOLD venographic (HRBV) imaging to stress the ability for visualizing the venous vasculature in the brain. A little later, an alternate acronym named AVID BOLD was suggested, where AVID stood for the application of venographic imaging to diagnose disease and BOLD for blood oxygenation level dependent imaging. Finally, the term susceptibility weighted imaging, or SWI for short, was introduced. The older acronyms can of course still be used if the goal is just to visualize the veins for vascular or anatomical purposes; however, one should be aware that they refer to a more specific subset of the more general concept of SWI.

Historically, the work developed from a focus on BOLD imaging. Due to Seiji Ogawa’s seminal papers on BOLD imaging in 1990 [1–3], the importance of a comprehensive understanding of the BOLD phenomena was soon understood. This led to a publication
expanding on the importance of this concept in 1993 [4], followed by papers on the topics of
high-resolution BOLD imaging [5], the size of the expected signal [6], and the role that the
venous blood played [7]. The next steps on this historical path included investigations on the
consistency of the BOLD effect [8], new ways to reveal its presence through the creation of
images showing the susceptibility-affected regions from other tissues [9], and investigations
of long echo time effects [10]. All this work with gradient echo imaging culminated in a
review of the topic [11]. Much of these efforts on understanding the early BOLD effect led to
the great vein/brain debate set off by discussions between Amos Hopkins and Mark Haacke,
then at Case Western Reserve University (who proposed that the major source of the BOLD
signal came from major veins), and Bruce Rosen and Jacques Belliveau (the early
investigators of the BOLD effect with an emphasis on diffusion effects) at Massachusetts
General Hospital [12]. The result of the thrust by the CWRU group was a demonstration that
veins played a major role in the BOLD effect from both intravascular and extravascular
perspectives. This work provided the early roots in identifying the importance of veins in
generating the BOLD effect and the concepts laid out in the paper of Lai et al. [4], and
eventually led to the focus on a better understanding of the sources of susceptibility and also
enhancing the visibility of the veins themselves. Prior to this, and often still mistakenly today,
people believed that it was diffusion around these gradients that led to the BOLD effect.

At this point in time, it had become clear that the phase of the complex MR signal could
reflect a major non-\$T_2^*$ -based beating effect. This was then used to collect high-resolution 3D
gradient echo data at the appropriate echo times to enhance the cancellation of the signal of
veins with brain parenchyma (see Figure 1.1). Thus was born the high-resolution BOLD
venographic, or HRBV, method [13].

During this period, as an improved understanding of the effects of oxygen saturation and
blood flow evolved, a new interleaved method was used to measure susceptibility and flow
almost simultaneously [14]. In this way, it was shown that venous oxygen saturation ($Y$
) deep in the brain was roughly 0.55 [14, 15]. With these experiments, it became clear that
phase could be used to distinguish arteries from veins. This possibility was first examined in
the leg (due to the fact that its vessels are almost parallel to the main magnetic field), where,
using the high-pass phase information, signal from veins could be separated from arteries,
even in the presence of a contrast agent [16].

About the same time, high-resolution capabilities demonstrated convincingly that
HRBV shows small veins better as the spatial resolution increases, giving an unprecedented
in vivo view of cerebral venous vessels heretofore only available from cadaver brain
studies [17].

Then a new direction of evaluating the BOLD effect was pursued where the signal
behavior was investigated in greater detail by applying multi-echo methods [18]. Still, the
role that other brain tissues played in the signal formation, especially cerebrospinal fluid,
was not clear, so some work was done on modeling the BOLD response [19–21].

In parallel to these developments that were more oriented toward basic research, HRBV
was also being tested for a number of interesting clinical applications (hence the move to a
new acronym AVID BOLD), including occult venous brain diseases [22, 23], arteriovenous
malformations [24], multiple sclerosis [25], brain tumors [26, 27], comparisons of activated
regions in functional MRI (fMRI) [28], and applications with respect to improved target
volume characterization and treatment planning in radiotherapy [29].

Methods were explored to further improve the image quality, such as reducing echo times
using a contrast agent [30]. This worked well for $T_1$ shortening agents because it increases
the signal from the blood pool and leads to larger cancellation effects. Another possibility
to improve image quality is to utilize the signal gain with higher field strengths and the HRBV concept was successfully extended to 3 T soon after [31]. Around the same time, the Ohio group started to use their 8 T scanner to acquire susceptibility weighted images at this ultrahigh field strength. They demonstrated with post mortem specimens that images with spatial resolutions of $0.25 \times 0.25 \times 2.0 \text{ mm}^3$ could depict vessels of less than 100 $\mu$m.

FIGURE 1.1  Phase images acquired at 3 T with echo times of (a) 12 ms, (b) 20 ms, (c) 40 ms, and (d) 60 ms. Most veins and cortical structures start to become visible even at the 12 ms echo time (equivalent to 24 ms TE at 1.5 T), and become more and more pronounced with longer echo times. However, the signal loss associated with $T_2^*$ effects due to extravascular field distortions around the veins also increases with echo time, making the apparent venous vessel diameter much larger than it is physically (this is also known as the blooming artifact). Hence, an echo time of 20 ms appears to provide a nice balance of good structural definition in phase with low concomitant $T_2^*$ loss.
in diameter [32]. It was also shown that phase rather than magnitude reconstruction can further improve these images at 8 T by providing not only improved depiction of the vasculature, but also better GM/WM contrast [33]. The topic of using phase images and employing unwrapping methods to improve the diagnostic value of HRBV was also investigated at lower field strengths (1.5 and 3 T) and resulted in high-quality brain venograms, even in regions where rapid susceptibility changes occur [34, 35]. More recently, SWI has been evaluated at 7 T [36], showing beautiful venograms and revealing even the smallest of veins: the venules (see Figure 1.2), which are similar to in vitro studies by Duvernoy et al. [37].

In 2004, the term susceptibility weighted imaging was coined to better stress the fact that susceptibility differences between tissues, which is different from spin density, T1- or T2-weighted imaging, can be utilized as a new type of contrast in MRI [38], and that the method is not necessarily restricted to visualizing veins in the brain. In fact, the areas of applications, to name a few, may range from enhancing gray matter/white matter contrast and water/fat contrast using phase information to identifying brain iron [39] or cerebrovascular malformations. Key to these possibilities is the utilization of magnetic susceptibility differences as they manifest themselves in local phase changes between tissues, and that the SWI high-pass filtered phase image is used either by itself as a new source of contrast and/or as a means of altering the contrast in the magnitude image. A simple example is given in Figure 1.3, although one will find many other examples throughout the book.

As it happens many times during the development of a new method or technique, the term introduced to describe the method has already been used before. Not surprisingly, this is also the case with the term susceptibility weighted imaging that has been used in the literature to describe data acquisition by using the magnitude information of conventional, $T_2^*$-weighted gradient echo images, which are mostly 2D with relatively long echo times and long repetition times. As an example, Ohnishi et al. applied this technique, which they
called susceptibility weighted gradient echo MR imaging [40], to investigate whether cerebral vasodilatory capacity can be shown by the acetazolamide challenge in healthy subjects and patients with chronic occlusive cerebrovascular disease. Also commonly known in the literature is the technique of dynamic contrast-enhanced susceptibility weighted imaging, which acquires $T_2^*$-weighted images to track the bolus of a contrast agent passing through the brain or any other organ, thereby leading to a signal intensity decrease because of a transient increase in susceptibility. This method has become a widely used tool for perfusion measurements and is usually performed with rapid gradient echo imaging or ultrafast echo planar imaging sequences. Under normal clinical conditions, only magnitude information is used with these sequences and phase information is discarded. Furthermore, acquisition speed is traded off against spatial resolution. However, technology continues to develop and resolution for EPI scans continues to improve (Figure 1.4). Even these methods can be used to obtain phase data that are subsequently processed to create what is referred to in this book as SWI filtered phase and processed SWI magnitude data.

Contrasting these developments, SWI, as it has evolved over the years, can now be considered an imaging method that combines the following features in a rather unique combination. It is based on high-resolution 3D gradient echo imaging (usually with full flow compensation in all three directions), where the 3D nature of the sequence allows for the acquisition of thin slices to reduce signal losses from background field inhomogeneities. Filtering the phase images removes unwanted field effects and phase wraps, generating an image contrast distinct from the magnitude image. A phase mask is created that is applied to the magnitude images, inherently combining the magnitude and phase contrast. Finally, a minimum intensity projection (mIP) is taken over adjacent contiguous slices. With this special data acquisition and image processing, it becomes possible to produce magnitude images with enhanced contrast that are exquisitely sensitive to venous blood, hemorrhage, or iron storage, and offer the potential to improve diagnosis of diseases and follow-up for
FIGURE 1.4 (a) MRA pre-Gd; (b) phase processed SWI post-Gd; (c) high-resolution perfusion weighted imaging (PWI) with the original cerebral blood volume (CBV) map; and (d) overlay of SWI data with PWI data in an attempt to remove the macrovessel contamination and reveal pristine gray matter and white matter. Image quality and contrast may not be optimal due to conversion from color to grayscale display. Please see the color plates section for the original version of this figure.
longitudinal studies. Of course, the SWI processed phase images themselves are of importance for quantifying iron [41] and for susceptibility mapping [39]. The latter is the final step of deconvolving phase into a susceptibility map. Although 3D data is preferred in the brain because of the vessels and small structures of interest, 2D breath-hold approaches are also possible in imaging the liver. The key feature for SWI is to use phase information for enhanced contrast and for local susceptibility information.

One frequently asked question concerning susceptibility weighted imaging is: “How is SWI different from conventional gradient echo imaging?” The answer to this lies in the use of the filtered phase as briefly discussed above. Let us therefore diverge a little bit into the physics of why a $T_2^*$-weighted sequence shows signal losses in the first place and why, for example as in Figure 1.5a, it does not show the veins as well as they are seen

![FIGURE 1.5](image1.png)

**(Figure 1.5)** (a) Original magnitude gradient echo image, (b) phase mask, and (c) final processed SWI data. Note the enhanced venous contrast obtained by using the phase mask.
on the filtered phase (Figure 1.5b) or on the SWI processed image itself (Figure 1.5c). First, it must be remembered that signal dephasing occurs because a phase spread exists across a voxel. Without phase dispersion, there is no extra \( T^*_2 \) effect. Therefore, tissues that have very low and uniform iron distribution, for instance, will show a phase effect, but not a \( T^*_2 \) effect. An example of this antithetic effect is shown for the stroke patient in Figure 1.6.

Now, performing gradient echo imaging with higher and higher spatial resolution, the phase dispersion across a voxel diminishes, and one sees less and less \( T^*_2 \) effects while the phase maintains its integrity. This is just as true at high field strengths, where, as long as the product of \( B_0 \cdot \text{TE} \) remains constant, the filtered phase images will look the same at all field strengths apart from signal-to-noise effects (see Chapter 20). Therefore, one would expect that the fully processed SWI data should show the veins much better than the original gradient echo magnitude images (see Figure 1.7).

An important precursor to the final processed SWI magnitude data is the creation of the filtered phase images. These images directly carry susceptibility information, although they are not yet a direct map of the actual susceptibility. Nevertheless, after processing the phase, the information seen on these images correlates well with veins and iron in the form of ferritin or hemosiderin in the brain. One interesting aspect, which is also covered in the following chapters and anticipated to have a major impact in the field of SWI, is the topic of susceptibility mapping and potentially quantifying magnetic susceptibility. Since the magnetic induction \( B \) determines the local precession frequency and is given by \( B = \mu_0 \cdot (H + M) = \mu_0 \cdot (1 + \chi) \cdot H \), any spatial variation in \( \chi \) is also reflected in the spatial variation of the Larmor frequency (see chapter 2 for more details). Therefore, it should be possible to relate directly the spatial variation of the MR frequency to the spatial variation of susceptibility. This is indeed readily possible for objects with simple geometries, such as cylinders, spheres, or plates. The problem, however, becomes more intricate for more complex susceptibility distributions, for which it is usually necessary to use numerical methods. Quite recently, efforts have been undertaken to calculate magnetic field perturbations via Fourier analysis of heterogeneous magnetic susceptibility distributions [42, 43]. Based on these approaches, it may become possible to calculate tissue susceptibilities from phase images, which, in turn, would be highly beneficial since magnetic susceptibility is an intrinsic tissue property that reflects tissue composition more closely than the phase image. Quantifying magnetic susceptibility of biological tissues in this way would have immediate important clinical implications, such as differentiating a hemorrhagic lesion as acute or chronic, identifying calcifications, or measuring oxygen saturation in the blood (see Figure 1.8). This susceptibility mapping concept will make it possible to quantify iron and even new iron-tagged contrast agents for molecular imaging.

The collection of topics in the following chapters demonstrates the plethora of possible applications both from a basic research point of view and from a clinical point of view.
of view. Written by experts in their respective fields, these topics comprise issues (among many others) such as the extraction of oxygen saturation, quantification of iron, applications to functional fMRI, and efforts in speeding up data acquisition, followed by a wide range of clinical applications in which SWI has already proven its potential.

FIGURE 1.7  (a) Pre-caffeine minimum intensity projection (mIP) over 20 slices with 2 mm thickness each. Visualization of the vessels is not particularly good. (b) A maximum intensity projection (MIP) over the high-pass filtered phase images for the same 20 slices. This image shows which parts of the magnitude image will be affected when the SWI data are processed. (c) Post-caffeine mIP over the same 20 slices. The visualization of the vessels has improved compared to (a) due to the vasoconstrictive effect of caffeine, although the image quality is not as good as the SWI processed data shown in (d). (d) The mIP of the fully processed SWI data demonstrating the venous system in great detail with excellent contrast.