Improving Susceptibility Mapping Using a Threshold-Based K-Space/Image Domain Iterative Reconstruction Approach

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To improve susceptibility quantification, a threshold-based k-space/image domain iterative approach that uses geometric information from the susceptibility map itself as a constraint to overcome the ill-posed nature of the inverse filter is introduced. Simulations were used to study the accuracy of the method and its robustness in the presence of noise. In vivo data were processed and analyzed using this method. Both simulations and in vivo results show that most streaking artifacts inside the susceptibility map caused by the ill-defined inverse filter were suppressed by the iterative approach. In simulated data, the bias toward lower mean susceptibility values inside vessels has been shown to decrease from around 10% to 2% when choosing an appropriate threshold value for the proposed iterative method. Typically, three iterations are sufficient for this approach to converge and this process takes less than 30 s to process a 512 × 512 × 256 dataset. This iterative method improves quantification of susceptibility inside vessels and reduces streaking artifacts throughout the brain for data collected from a single-orientation acquisition. This approach has been applied to vessels alone as well as to vessels and other structures with lower susceptibility to generate whole brain susceptibility maps with significantly reduced streaking artifacts. Magn Reson Med 69:1396–1407, 2013. © 2012 Wiley Periodicals, Inc.

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Susceptibility weighted imaging (SWI) using phase information has become an important clinical tool (1–3). However, the use of phase information itself has stimulated great interest both as a source of contrast (4–6) and a source for producing susceptibility maps (SM) (7–24). The impetus for solving the inverse problem from magnetic field perturbation came from the work described by Deville et al. (25). This was noted by Marques and Botev (14,20,22,23) have shown good overall results, but they require longer reconstruction times and assumptions about the contrast in or near the object to be detected. Threshold-based, single-orientation regularization methods (TBSO) (11,15,18,24) provide the least acquisition time and the shortest computational time to calculate SM. However, their calculated SMs lead to underestimated susceptibility values (Δχ) and display severe streaking artifacts especially around structures with large Δχ, such as veins or parts of the basal ganglia.

Based on TBSO approaches, we propose an iterative method to overcome the singularities in the inverse filter and produce improved accuracy for susceptibility mapping. In this approach, we iteratively replace k-space values associated with the SM, χ(k), near the singularities to obtain an almost artifact free SM, χ(r). The k-space values used for substitutions are estimated using structural information from the masked version of χ(r). Simulations using 2D cylinders and full brain 3D models were performed to examine the efficiency of this iterative approach. High resolution human data are also evaluated.

METHODS

Briefly, the expression for the susceptibility distribution (26,27) derived from the phase data can be written as (for a right handed system (28)):

\[ χ(r) = FT^{-1} \left[ \frac{1}{g(k)} \times FT \left[ \frac{Φ(r)}{-γB_0 T_E} \right] \right] \]  \[ \text{[1]} \]

where,

\[ g(k) = \frac{1}{3} - \frac{k_x^2}{k_x^2 + k_y^2 + k_z^2} \]  \[ \text{[2]} \]

and Φ(r) is the phase distribution, T_E is the echo time, γ is the gyromagnetic ratio for hydrogen protons, B_0 is the main field strength, k_x, k_y, and k_z are coordinates in k-space, and g(k) is the Green’s function or filter. Clearly, the analytic inverse filter g^{-1}(k) = 1/g(k), is ill-posed when g(k) is equal or close to zero, i.e., points on or near two conical surfaces in k-space at the magic angles of 54.7° and 125.3° from the B_0 axis. This ill-posedness leads to severe artifacts (including severe streaking) in
Susceptibility Mapping Using Iterative Approach

The geometry of the structures of interest is discussed below and shown in Fig. 1.

K-space Iterative Approach

If the shapes of the structures of interest are known, then one can use this information in the SM to create a more accurate k-space of said SM in the conical region. The structure of the vessels is obtained directly from the first pass SM $\chi_{i=0}(r)$. The detailed steps of the iterative method are discussed below and shown in Fig. 1.

• **Step-1:** An initial estimate of the SM, $\chi_{i=0}(r)$, is obtained by applying a regularized version of the threshold-based inverse filter, $g_{reg}(k)$ (18), in Eq. 1 using the suggested threshold value, $\text{thr} = 0.1$. The subscript “$i$” denotes the SM after the $i$th iteration (“$i = 0$” denotes the initial step before doing the iterative method and $i = 1$ for the first iteration).

• **Step-2:** The geometry of the structures of interest is extracted from $\chi_{i=0}(r)$ using a binary vessel mask, i.e. outside the veins, the signal in the mask is set to zero, and inside it is set to unity. Since streaking artifacts associated with veins in the SM are usually outside the vessels, after multiplying the $\chi_i(r)$ map by the mask, little streaking remains in the SM. This leads to $\chi_{vm,i}(r)$ as shown in Fig. 1b. Vessel mask generation will be addressed in the next section.

• **Step-3:** $\chi_{vm,i}(k)$ is obtained by Fourier transformation of $\chi_{vm,i}(r)$ (Fig. 1c).

• **Step-4:** The predefined ill-posed region of k-space in $\chi_{vm,i}(k)$ is extracted (Fig. 1d). These extracted k-space data are denoted by $\chi_{vm,cone}(k)$. The size of $\chi_{vm,cone}(k)$ is decided by a threshold value, $a$, which is assigned to $g(k)$. For the matrix size $512 \times 512 \times 512$, the percentages of the cone region in k-space for a given $a$, are 2.4% ($a = 0.01$), 24.1% ($a = 0.1$), 47.1% ($a = 0.2$), and 70.6% ($a = 0.3$), respectively. When $a$ increases, the size of $\chi_{vm,cone}(k)$ increases too. If $a$ is increased too much then most of the original information will be lost.

• **Step-5:** Data from $\chi_{vm,cone}(k)$ and $\chi_{i=0}(k)$ (Fig. 1e) are merged. This means part of $\chi_{i=0}(k)$ has been replaced by $\chi_{vm,cone}(k)$. The merged data are denoted by $\chi_{merged,i}(k)$ (Fig. 1f).

• **Step-6:** Inverse Fourier transformation of $\chi_{merged,i}(k)$ gives the improved SM, $\chi_{i+1}(r)$ (Fig. 1g).

• **Step-7:** $\chi(r)$ in step-1 is replaced by $\chi_{i+1}(r)$ from step-6 and the algorithm is repeated until

$$\sqrt{\sum [(\chi(r) - \chi_{i+1}(r))^2]/N} < \varepsilon$$

where $N$ is the number of pixels in $\chi(r)$ and $\varepsilon$ is the tolerance value (chosen here to be 0.004 ppm).

Binary Vessel Mask Generation

The binary vessel mask was generated using thresholding from the $\chi(r)$ map itself. The detailed steps are discussed below and shown in Fig. 2.

• **Step-1:** A threshold, $\text{th}_1$, is applied to $\chi_{i=0}(r)$ to create an initial binary vessel mask, $M_0$. The pixels whose susceptibility values are lower than $\text{th}_1$ will be set to zero while those greater than or equal to $\text{th}_1$ will be set to unity. In this study, a relatively low susceptibility of 0.07 ppm is used for $\text{th}_1$ to capture most vessels. However, this choice of threshold inevitably includes other brain structures in $M_0$ that have high susceptibility.

• **Step-2:** A morphological closing operation is performed to fill in holes in $M_0$ to generate an updated mask $M_1$. 

\[\chi(k)\] and noise amplification (29). Thus, for a proper pixel-by-pixel reconstruction of $\chi(r)$, recovering the correct values of $\chi(k)$ near the region of singularities is critical.
• **Step-3:** A median filter is applied to remove noise in \( M_1 \) and create \( M_2 \).

• **Step-4:** False positive data points from \( M_2 \) are removed as follows: First, the \( \chi(r) \) map is mipped over five slices centered about the slice of interest to better obtain contiguous vessel information, as seen in \( \chi_{\text{MIP}}(r) \). Second, another threshold, \( \text{th}_2 = 0.25 \) ppm, is performed on \( \chi_{\text{MIP}}(r) \) to create a new \( \chi_{\text{MIP,vm}}(r) \) and binary mask \( M_P \), which only contains predominantly vessels. Here, 0.25 ppm was chosen to isolate the major vessels in the MIP image. Third, each slice from \( M_2 \) is compared with \( M_P \) on a pixel-by-pixel basis to create \( M_3 \). If a data point from \( M_2 \) does not appear on \( M_P \), this data point will be treated as a false positive and removed from \( M_2 \), otherwise this point is retained. This process can be equally well applied to extract other tissues by choosing appropriate values for \( \text{th}_1 \) and \( \text{th}_2 \).

### 2D Cylinder Simulations

Simulation of a two dimensional cylinder and its induced phase was first performed using a 8192 x 8192 matrix. A lower resolution complex image was then obtained by taking the Fourier transform of this matrix and applying an inverse Fourier transform of the central 512 x 512 matrix in k-space. This procedure is to simulate Gibbs ringing effects caused by finite sampling which we usually see in conventionally required MR data sets. Gibbs ringing comes from discontinuities in both the magnitude and phase images. To avoid Gibbs ringing from magnitude discontinuities, we used a magnitude image with a uniform signal of unity. Cylinders with diameters 32, 64, 128, 256, 512, and 1024 were simulated on 8192 x 8192 matrices and their effective diameters were 2, 4, 8, 16, 32, and 64 on 512 x 512 matrices. All phase simulations were performed using a forward method (8,26,27,30) with \( B_0 = 3 \) T, \( \Delta \chi = 0.45 \) ppm in SI units, \( T_E = 5 \) ms, and the cylinder perpendicular to the main magnetic field. The susceptibility value of 0.45 ppm represents venous blood when the hematocrit (Hct) = 0.44, \( \Delta \chi_{\text{do}} = 4\pi \times 0.27 \) ppm (31) and the oxygen saturation level = 70%, where \( \Delta \chi_{\text{do}} \) is the susceptibility difference between fully deoxygenated and fully oxygenated blood (32). A relatively short echo time was chosen to avoid phase aliasing that can affect the estimated susceptibility values.

### Selection of a TBSO Method to Generate the \( \chi_{\text{i-o}}(r) \) Map

TBSO methods (11,15,18,24) use a truncated \( g(k) \) to solve the singularity problem in the inverse filter \( g^{-1}(k) \) when \( g(k) \) is less than a predetermined threshold value, \( \text{thr} \). When \( g(k) < \text{thr} \), \( g^{-1}(k) \) is either set to zero (11,24); or to \( 1/\text{thr} \) (15); or set to \( g^{-1}(k) = 1/\text{thr} \) first and then \( g^{-1}(k) \) is brought smoothly to zero as \( k \) approaches \( k_{\text{so}} \). This smoothing is accomplished by multiplying \( g^{-1}(k) \) by \( \alpha^2(k_z) \) with \( \alpha(k_z) = (k_z - k_{so})/|k_z - k_{so}| \) where \( k_z \) is the \( z \) component of that particular point in k-space, \( k_{so} \) is the point at which the function \( g^{-1}(k) \) becomes undefined, and \( k_{so} \) is the \( k_z \) coordinate value where \( |g(k)| = \text{thr} \) (18).

SMs using the methods in Refs. 11,15,18 were calculated based on Eq. 1 using the 2D cylindrical model. Equation 1 can be used to calculate the SM for the simulated 2D cylinder model perpendicular to the main field since the 2D perpendicular model is a special case of the 3D model with 1 slice [10]. Streaking artifacts are obvious in all three SMs (figures are not shown). The calculated mean susceptibility values inside the cylinder
The effect of high-pass (HP) filtering the phase data on enhancement from the inversion process.

correlate noise in the phase with the expected noise measured in the phase image (i.e., so we can from all major sources of streaking artifacts to compare the ground noise in the SM is measured in a region away to measure streaking artifacts outside the cylinder. Back-

Finding an Optimal Threshold Value

To find the optimal threshold, a series of $\chi(r)$ maps were reconstructed by the iterative method using threshold values $a$ of 0.01, 0.03, 0.07, 0.1, 0.15, 0.2, 0.25, and 0.3. The larger this threshold, the closer the final estimate for $\chi(r)$ will be to $\chi_{\text{true}}(r)$. The optimal threshold value was found by comparing the accuracy of the estimated susceptibility values as well as the effects on reducing streaking artifacts in the reconstructed $\chi(r)$ maps. To study the effect of noise in $\chi(r)$ maps due to the noise in phase images, complex datasets for cylinders of diameter 2, 4, 8, 32 voxels, respectively, were simulated with Gaussian noise added to both real and imaginary channels. Noise was added in the complex images to simulate a SNR-magnitude of 40:1, 20:1, 10:1, and 5:1 in the magnitude images. Since $\sigma_{\text{phase}} = 1/\text{SNR-magnitude}$, this corresponds to $\sigma_{\text{phase}} = 0.025, 0.05, 0.1, \text{and } 0.2 \text{ radian}$.

To estimate the improvement in the SM by the iterative method, we used a root mean squared error (RMSE) to measure streaking artifacts outside the cylinder. Background noise in the SM is measured in a region away from all major sources of streaking artifacts to compare the noise measured in the phase image (i.e., so we can correlate noise in the phase with the expected noise enhancement from the inversion process).

Effect of High-Pass Filter

The effect of high-pass (HP) filtering the phase data on the $\chi(r)$ map generated by the iterative method was also studied. Phase images of a cylindrical geometry with diameters of 2, 4, 8, 16, 32, and 64 voxels were simulated. Homodyne HP filters (33) with a 2D hanning filter (full width at half-maximum, FWHM = 4, 8, 16, and 32 pixels) were applied on these phase images in both in-plane directions. SM reconstructions were stopped based on the criteria in step 7 of the iterative process.

Three Dimensional Brain Model Simulations

To address the potential of the iterative technique to improve the SM of general structures such as the basal ganglia, a 3D model of the brain was created including the: red nucleus (RN), substantia nigra (SN), crus cerebri (CC), thalamus (TH), caudate nucleus (CN), putamen (PUT), globus pallidus (GP), gray matter (GM), white matter (WM), cerebrospinal fluid (CSF), and the major vessels (34). The structures in the 3D brain model were extracted from two human 3D $T_1$ weighted and $T_2$ weighted data sets. Basal ganglia and vessels are from one person; GM and WM are from the other person’s data set. Since all structures are from in vivo human data sets, this brain model represents realistic shapes and positions of the structures in the brain. Susceptibility values in parts per million (ppm) for the structures SN, RN, PUT, and GP, were taken from Ref. 12 and others were from measuring the mean susceptibility value in a particular region from SMs using Ref. 18 from in vivo human data: RN = 0.13, SN = 0.16, CC = −0.03, TH = 0.01, CN = 0.06, PUT = 0.09, GP = 0.18, vessels = 0.45, GM = 0.02, CSF = −0.014, and WM=0. All structures were set inside a 512 × 512 × 256 matrix of zeros. The phase of the 3D brain model was created by applying the forward method (8,26,27,30) to the 3D brain model with different susceptibility distributions using the imaging parameters: $T_E = 5 \text{ ms}$ and $B_0 = 3 \text{ T}$. A comparison between the phase maps from this brain model and a real data set is shown in Fig. 3. To match the imaging parameters of the real data set, $B_0 = 3 \text{ T}$ and $T_E = 18 \text{ ms}$ were applied for the results presented in Fig. 3. Except for Fig. 3, all other figures in the paper associated with the 3D brain were simulated by using $T_E = 5 \text{ ms}$.

In Vivo MR Data Collection and Processing

A standard high-resolution 3D gradient echo SWI sequence was used for data acquisition. A transverse 0.5 mm isotropic resolution brain dataset was collected at 3 T from a 23-year-old healthy volunteer. The sequence parameters were: TR = 26 ms, flip angle = 15°, read
bandwidth = 121 Hz/pixel, $T_E = 14.3$ ms, 192 slices, and a matrix size of $512 \times 368$. To reconstruct $\chi_{\text{io}}(r)$ with minimal artifacts, the following steps were carried out:

1. The unwanted background phase variations were removed using either: (a) a homodyne HP filter (FWHM = 16 pixels) (33) or (b) Prelude in FMRIB Software Library (FSL) (35) to unwrap the phase, followed by the process of Sophisticated Harmonic Artifact Reduction for Phase data (SHARP) (36) with a filter radius of 6 pixels. To reduce artifacts in the calculated SMs, regions with the highest phase deviations due to air/tissue interfaces were removed manually from the HP filtered phase images and the phase in those regions were set to zero.

2. A complex threshold approach (37) was used to separate the brain from the skull.

3. The phase image with an original matrix size of $512 \times 368 \times 192$ was zero filled to $512 \times 512 \times 256$ to increase the field-of-view and to avoid streaking artifacts caused by the edge of brain to alias back to the reconstructed SM.

4. The regularized inverse filter, $g_\text{reg}^{-1}(k)$ (18) was applied to obtain $\chi_{\text{i0}}(r)$, followed by the iterative process using $a = 0.1$. For in vivo data, the iterative program was terminated at the third iterative step.

RESULTS

Selection of Threshold Level Based on Simulations

To find the optimal threshold value, SMs were reconstructed using $a = 0.01, 0.03, 0.07, 0.1, 0.15, 0.2, 0.25,$ and 0.3, respectively, with different noise levels (Fig. 4). The streaking artifacts shown in $\chi_{\text{i0}}(r)$ (the first column in Fig. 4a) have been significantly reduced by the iterative method and fall below the noise level when $a >= 0.1$. Also, when $a >= 0.1$, the mean susceptibility value

FIG. 4. Simulations showing the comparison of the calculated susceptibility distributions for a cylinder perpendicular to $B_0$ at different threshold values ($a$) applied to $g(k)$ as well as the initial $\chi_{\text{i0}}(r)$ map. The direction of $B_0$ is indicated by a black long arrow. The susceptibility, $\Delta \chi$, inside the cylinder is 0.45 ppm. a: The comparison of the converged $\chi_{\text{i0}}(r)$ map with the $\chi_{\text{i0}}(r)$ map for a diameter of 32-pixel cylinder, where $b$ is the iterative step required to reach convergence. In this data, $b = 2$ when $a = 0.03$, $b = 3$ when $a = 0.1$ and $b = 4$ when $a = 0.2$ when $\sigma_{\text{phase}} = 0$. The top row of images shows simulations with no phase noise. The second and the third row show simulations with added phase noises $\sigma_{\text{phase}} = 0.025$ and 0.05 radian, respectively. The first column of images show initial $\chi_{\text{i0}}(r)$ maps for reference. b: The variation of the mean calculated susceptibility inside the cylinder with different threshold value, $a$, for diameter ($d$) = 2, 4, 8, and 32 pixels cylinders. The mean susceptibility value is independent of the noise level; therefore, only mean values from $\sigma_{\text{phase}} = 0$ were provided. c: The variation of the RMSE of the susceptibility values outside the cylinder as a function of the threshold value, $a$, and the noise level. The $d = 32$ pixels cylinder was used to generate (c). The range of the gray-scale bars is chosen to highlight the artifacts in the images. It does not reflect the quantified higher susceptibility values inside cylinders.
inside the cylinder was found to increase to 0.44 ppm when the diameter of the cylinder was larger than 8 pixels (Fig. 4b) and this trend is independent of the object size and the noise in the phase image. The optimal result in terms of obtaining the true susceptibility value was with a threshold of 0.1. Figure 4c shows a plot of RMSE of the susceptibility values from the whole region outside the 32-pixel cylinder using different a. The RMSE of the susceptibility values decreases as a increases. Therefore, for vessels, a value of a = 0.3 would be the optimal value. However, a large threshold value means replacing more original k-space with the k-space only side the 32-pixel cylinder using different a.

The inverse process (18) was applied to the dipole field reduction in thermal noise contribution. indicated by the black circle in Fig. 4a. The overall was measured in a region outside the streaking artifact. Since the SM using signals from other brain structures and blur these structures. Therefore, for vessels, a value of a = 0.1 already reveals the optimal susceptibility value for the vessels and an acceptable RMSE, it is appropriate to choose 0.1 for more general applications to study the entire brain.

Figure 4a compares the converged \( \chi_{\text{inv}}(r) \) map with the \( \chi_{\text{inv}}(r) \) map, where \( b \) is the iterative step required to reach convergence. In this data, \( b = 2 \) when \( a = 0.01 \) and 0.03, \( b = 3 \) when \( a = 0.07, 0.1, \) and 0.15 and \( b = 4 \) when \( a = 0.2, 0.25, \) and 0.3 for \( \sigma_{\text{phase}} = 0 \). When \( \sigma_{\text{phase}} \) increases, more iterative steps were required to reach convergence. For instance, the maximum iterative step number is 9 when \( \sigma_{\text{phase}} = 0.2 \) radians. Using a noise level of 0.025 radian in the phase image as an example, \( g_{\text{reg}}(k) \) (18) leads to a susceptibility noise of roughly 0.025 ppm in the \( \chi_{\text{inv}}(r) \) map. The iterative approach leads to a slight decrease in background noise, 0.021 ppm, in \( \chi_{\text{inv}}(r) \) when \( a = 0.1 \). The background noise was measured in a region outside the streaking artifact indicated by the black circle in Fig. 4a. The overall decrease in RMSE in the background (Fig. 4c) is a consequence of both a decrease in streaking artifacts and a reduction in thermal noise contribution.

Selection of the Optimal Iterative Step

The inverse process (18) was applied to the dipole field in Fig. 5a to give the \( \chi_{\text{inv}}(r) \) map shown in Fig. 5b; prominent streaking artifacts are evident in this image. Streaking artifacts are significantly reduced at each step of the iterative method quickly reaching convergence (Fig. 5c–e). The largest improvement is seen in the first iterative step, which is verified by Fig. 5f, showing the difference between Fig. 5c (\( \chi_{\text{inv}}(r) \) map) and Fig. 5b (\( \chi_{\text{inv}}(r) \) map). After the second iteration, we can see some minor streaking reductions (Fig. 5g, the difference between the \( \chi_{\text{inv}}(r) \) map and \( \chi_{\text{inv}}(r) \) map). The mean susceptibility value approaches 0.44 ppm in a single step. Similar results (not shown) are also obtained when the iterative method is run with different aspect ratios between the in-plane resolution and the through plane resolution (such as 1:2 and 1:4). The iterative approach always lead to higher final susceptibility values compared to the initial value in \( \chi_{\text{inv}}(r) \). Finally, even when an HP filter is applied, up to a 10% increase in the susceptibility is realized (Fig. 5i). The SMs of large vessels benefit from a low order HP filter (FWHM = 4 pixels) and small vessels up to 8 pixels benefit from a HP filter (FWHM = 16 pixels).

Effect of the Iterative Approach on Surrounding Brain Tissues in the 3D Brain Model

SM Reconstruction Using a Vessel Mask Only

Figure 6a,d represents \( \chi_{\text{inv}}(r) \), without noise and with 0.025 radians of noise in phase images. Figure 6f is the vessel map. Streaking artifacts (delineated by the black arrows) are obvious in Fig. 6a,d and significantly reduced in the \( \chi_{\text{inv}}(r) \) maps (Fig. 6b,e) using \( a = 0.1 \). Figure 6c is the \( \chi_{\text{inv}}(r) \) map using \( a = 0.2 \). As can be seen, when \( a \) increases, the iterative method still works for vessels, but brain tissues become more blurred. Figure 7a plots the mean susceptibility values inside the vessel (vein of Galen), GP, SN, RN, PUT, and CN from \( \chi_{\text{inv}}(r) \) maps generated by using \( a = 0.1, 0.15, 0.2, 0.25, \) and 0.3, respectively. The susceptibility value in the brain model and \( \chi_{\text{inv}}(r) \) map are also provided in the plot as references. Generally, the susceptibility values of brain tissues except vessels decrease as \( a \) increases while, for vessels, the susceptibility value is 0.41 ppm in the \( \chi_{\text{inv}}(r) \) map and is increased to 0.45 ppm in the \( \chi_{\text{inv}}(r) \) maps.

SM Reconstruction Using a Mask Including Vessels and Brain Structures

The iterative method is not limited to improving SM from just vessels; it can also be applied to the entire brain. Figure 6g shows a coronal view of the \( \chi_{\text{inv}}(r) \) map for the brain model. The \( \chi_{\text{inv}}(r) \) map using a mask keeping all major structures (GP, SN, RN, PUT, CN) and vessels is shown in Fig. 6h. In practice, this is equivalent to setting thresholds in the \( \chi_{\text{inv}}(r) \) map to be greater than 0.09 ppm to extract all these high susceptibility structures from the \( \chi_{\text{inv}}(r) \) map to create the mask. Figure 6h reveals that streaking artifacts associated with veins as well as all major structures have been reduced. Figure 6i shows the difference between Fig. 6g, h. In addition, streaking artifacts sometimes cause the appearance of “false” structures. For instance, there is no internal capsule (IC) included in the model (Fig. 6i), yet we see an IC like structure in the \( \chi_{\text{inv}}(r) \) map (Fig. 6j) (indicated by a dashed white arrow in Fig. 6j). The iterative method removes the streaking artifacts and the “false” IC (Fig. 6k). Figure 7b shows susceptibility values in each structure in the brain model for \( \chi_{\text{inv}}(r) \) map. The mask includes vessels and all major structures. The underestimated susceptibility values of all major structures and vessels in the \( \chi_{\text{inv}}(r) \) map have been recovered by the iterative method in the \( \chi_{\text{inv}}(r) \) map.

Effect of Errors in the Vessel Map

Accurately extracting vessels from \( \chi_{\text{inv}}(r) \) is critical for the iterative method. Figure 8b–d and the corresponding enlarged views (Fig. 8f–h) from the rectangular region indicated in Fig. 8a show the \( \chi_{\text{inv}}(r) \) maps using an accurate (Fig. 8j), a dilated (Fig. 8k), and an eroded (Fig. 8l) vessel map to show the effect of errors in the vessel mask on the \( \chi_{\text{inv}}(r) \) map. The dilated and eroded vessel maps were generated using Matlab functions based on a 3-by-3 square structuring element object. The susceptibility values measured from a vein indicated by the white arrow in Fig. 8e are 0.40 ± 0.03 ppm (Fig. 8e),...
0.45 \pm 0.03 \text{ ppm (Fig. 8f)}, 0.45 \pm 0.03 \text{ ppm (Fig. 8g)}, and 0.40 \pm 0.07 \text{ ppm (Fig. 8h)}, respectively. The iterative method still works if the vessel is slightly enlarged but does little to change the original \( x^{(0)}(r) \) map if the vessels are too small or absent in the mask. As we just discussed, streaking artifacts produced “false” vessels indicated by the dashed black arrow in Fig. 8e since these vessels are not in the model (Fig. 8i). These false vessels disappeared in Fig. 8f.

Results from the In Vivo Dataset

In the in vivo example, we compare the differences between SHARP (Fig. 9a–d) and a homodyne HP filter (FWHM = 16 pixels) (Fig. 9e–h). Compared to the transverse view, streaking artifacts are more obvious in the sagittal or coronal view. Figure 9a shows the \( x^{(0)}(r) \) map with severe streaking artifacts. The streaking artifacts were significantly reduced in the \( x^{(3)}(r) \) map (Fig. 9b) using \( a = 0.1 \). The streaking artifacts associated with the superior sagittal sinus vein (indicated by two black arrows in Fig. 9a) were significantly decreased in Fig. 9b,d. The subtracted image (Fig. 9c), Fig. 9a minus Fig. 9b, reveals the removed streaking artifacts. These streaking artifacts are one of the reasons why the \( x^{(0)}(r) \) maps appear noisy. In the \( x^{(3)}(r) \) map, the reduction in streaking artifacts from individual veins leads to a decrease of noise therefore an increased SNR of veins. If veins are the only interest, even a threshold of 0.2 can work reasonably well (Fig. 9d). Two relatively big veins, V1 and V2, indicated by the white dashed and white solid arrows, respectively, in Fig. 9b, were chosen to measure the susceptibility values. Results are provided in Table 1. The susceptibility values of these two veins have been improved by roughly 16% by the iterative method. The standard deviation of the susceptibility values measured
from a uniform region inside the WM decreased from 0.042 ppm in $\chi_{r=0}(r)$ map to 0.035 ppm and 0.023 ppm in the $\chi_{r=3}(r)$ map with $a = 0.1$ and 0.2, respectively. The baseline susceptibilities of the major structures are higher with SHARP than with the HP filter. The iterative method works for brain structures too when the structure is included in the mask. For instance, the mean susceptibility values of the GP and SN have been increased from $0.155 \pm 0.058$ ppm and $0.162 \pm 0.067$ ppm in the $\chi_{r=0}(r)$ map to $0.163 \pm 0.070$ ppm and $0.186 \pm 0.083$ ppm in the $\chi_{r=3}(r)$ map, from the dataset processed using SHARP. The result after HP filtering (Fig. 9e) shows more edge artifacts indicated by the left arrow in Fig. 9e. Much of this error was reduced by the iterative method (Fig. 9f). It seems that the iterative method compensated for the worse first guess (Fig. 9e) and ended up with almost the same result (Fig. 9f,h) as having started with SHARP (Fig. 9b,d) from the image perspective. Since a
small sized HP filter cannot remove rapid phase wrapping at air-tissue interfaces; we had to cut out the region near the sinuses in the phase images.

DISCUSSION

In this article, a threshold-based k-space/image domain iterative approach has been presented. Simulations and in vivo results show that the ill-posed problems of streaking artifacts and biases in the estimates of susceptibilities can be significantly reduced. The replacement of the \( \chi(k) \) values near the singularities by \( \chi_{vm}(k) \), which is obtained from the geometric information from the \( \chi(r) \) map itself, obviates many of the current problems seen in the TBSO methods. Since \( \chi_{vm}(r) \) contains little streaking artifacts itself, the values used inside the thresholded regions in \( \chi(k) \) now contain no artifact either. In this sense, we obtain an almost perfect k-space without bad data points in the region of singularities. This explains why this method converges quickly and the major improvement is in the first iterative step (Fig. 5).

The proposed iterative approach is different from the other threshold-based methods (11,15,18,19,24) which fill a predefined conical region using a constant, zero or \( 1/\text{thr} \) threshold (11,15,24) or the first-order derivative of \( g^{-1}(k) \) (19). The iterative method uses full geometry information from the SM (vessels or predefined structures and not edge information) to iteratively change k-space values in the conical region using the forward model. This is also quite different than other currently proposed solutions (9,12,20,22). Even though spatial priors such as gradients of the magnitude are used (9,12,20,22), in those methods, the meaningful values of the singularity regions in k-space are obtained through solving the complex cost function problem. However, the iterative method uses priors not from the magnitude image but from the SM. The missing data in the singularity regions are obtained through iterating back and forth between

![FIG. 7. The plots of mean susceptibility values inside the vessel (vein of Galen), GP, SN, RN, PUT, and CN from \( \chi_{3}(r) \) maps. The first two data points of each curve is the value inside each structure from the brain model and the \( \chi_{0}(r) \) map, respectively. a: \( \chi_{3}(r) \) maps generated by applying a region of interest map which consists only vessels using \( \alpha = 0.1, 0.15, 0.2, 0.25, \) and 0.3, respectively. b: \( \chi_{3}(r) \) maps generated by applying a region of interest map which consists of the GP, SN, RN, PUT, CN, and vessels using \( \alpha = 0.1 \).](image1)

![FIG. 8. Comparison of the reconstructed \( \chi_{3}(r) \) maps using (j) accurate, (k) dilated, and (l) eroded vessel maps. Their corresponding vessel maps and the enlarged views from the rectangular regions are provided in (b)-(d) and (f)-(h). (a) and (e) The initial \( \chi_{0}(r) \) maps and (i) the original brain model as references. The circle in the midbrain in the \( \chi(r) \) maps represents the RN and is indicated by a black arrow in (i). Other hyper-intense regions in SMs are vessels.](image2)
the SMs and their k-space. The advantage of cost function approaches is that they do not need to predefine the singularity region in k-space which is solved by the optimization process automatically (although the optimization process itself is usually quite time-consuming). On the other hand, the iterative method is the most time-efficient. It is fast enough to reconstruct SMs for a 512 × 512 × 256 data set using an Intel Core i7 CPU 3.4 GHz processor in less than 30 s, since in practice usually three iterations are good enough to generate decent results.

The threshold value also plays a key role. A threshold value of 0.1 is a reasonable choice since a lower threshold value leads to an increase in noise and a higher threshold value leads to a blurring of the object (Figs. 6c, 9d, h).

It is known that the ill-posedness of the inverse filter will increase the noise level from the phase to the SM. Based on both simulations and real data, we find that there is a factor of 4 increase in noise in the SM relative to the original phase data. This result and the fact at $B_0 = 3$ T, $T_E = 5$ ms, and $\sigma_{\chi_{\text{i}-0}(r)} = 0.025$ ppm make it possible to write the total noise in the background region in $\chi_{\text{i}-0}(r)$ as $0.025 \times (3/B_0) \times (5/T_E)$ in ppm. The noise in $\chi_{\text{i}-3}(r)$ will be less than this value since the iterative method will reduce streaking artifact in SM.

The iterative method can be used to remove streaking artifacts associated with not only vessels but also other

FIG. 9. Comparisons of SMs using SHARP or a HP filter (FWHM = 16 pixels) to remove the background field. The iterative method with $a = 0.1$ and $0.2$ is applied after the background is removed. (a)–(d) and (e)–(h) are results after the application of SHARP and the HP filter, respectively. (a) and (e) the initial $\chi_{\text{i}-0}(r)$ maps. (b) and (f) the $\chi_{\text{i}-3}(r)$ maps generated from the iterative method with $a = 0.1$. (c) and (g) the differences of images between (a) and (b), and between (e) and (f), respectively. These two images show the successful reduction of the streaking artifacts. (d) and (h) the $\chi_{\text{i}-3}(r)$ maps generated from the iterative method with $a = 0.2$. The range of the grayscale bars is chosen to highlight the artifacts in the images. It does not reflect the quantified susceptibility values inside veins.
Brain structures as well. Figure 6h shows a reduction in artifacts associated specifically with iron-rich regions such as the GP and CN.

Accurately extracting vessels from the $\chi_{x=0}(r)$ map is critical for the iterative method (Fig. 8). In this study, vessels were segmented directly from the SM (Fig. 2). It may also possible to segment veins from original magnitude images (9,12,20,22), phase images, and/or SWI images. Extraction of accurate anatomic information from phase data sometimes is difficult since phase is orientation dependent and phase changes are generally nonlocal. SWI images work better for an anisotropic dataset rather than an isotropic dataset since phase cancellation is needed to highlight vessel information. Therefore, we may consider combining SMs with magnitude images, phase images, and/or SWI images together to segment the veins, since different types of images can compensate for missing information.

The iterative method appears to help even in the presence of non-isotropic resolution with partial volume effects and to a minor degree when an HP filter is applied. A smaller sized HP filter would be better, since a larger HP filter will significantly underestimate the susceptibility value (Table 1). SHARP gave us better results compared with the HP filter (FWHM = 16 pixels) (Fig. 9), but SHARP requires phase unwrapping which can be time consuming and is noise dependent (19). From this perspective, an HP filter has the advantage since it does not need unwrapped phase. If the forward modeling approach of Neelavalli et al. (38) can be used to reduce air/tissue interface fields, then it may be possible to use a small size HP filter (FWHM = 8 pixels) which may provide similar results to SHARP.

Severe streaking artifacts associated with structures having high susceptibility values such as veins can lead to major changes in the appearance of the brain structures with low susceptibility. Practically, the susceptibility of the veins is a factor of 2.5–20 times higher than other structures in the brain. Therefore, even a 10% streaking artifact can overwhelm the information in the rest of the brain and create false appearing structures as in (Fig. 6j) and in (Fig. 8e). The reduction of these artifacts makes a dramatic difference in the ability to properly extract the susceptibility of other tissues.

In conclusion, both simulations and human studies have demonstrated that the proposed iterative approach can dramatically reduce streaking artifacts and improve the accuracy of susceptibility quantification inside the structures of interest such as veins or other brain tissues.

### Table 1

<table>
<thead>
<tr>
<th>$\chi_{x=0}(r)$</th>
<th>$\chi_{y=3}(r)$</th>
<th>$\chi_{z=3}(r)$</th>
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<tr>
<td>V1 (SHARP) 0.32 ± 0.07 0.37 ± 0.08 0.38 ± 0.09</td>
<td>V1 (HP) 0.24 ± 0.05 0.28 ± 0.06 0.28 ± 0.06</td>
<td>V2 (SHARP) 0.35 ± 0.04 0.40 ± 0.05 0.41 ± 0.05</td>
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<tr>
<td>V2 (HP) 0.25 ± 0.05 0.31 ± 0.06 0.30 ± 0.06</td>
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Mean and standard deviation for the susceptibility values (in ppm) of two veins processed using SHARP and a HP filter (FWHM = 16 pixels), respectively, were chosen from the 0.5 mm isotropic resolution data. V1 and V2 are shown in Fig. 9. The susceptibility values of these two veins have been increased by the iterative method. There is not much variation of the susceptibility value with different threshold values.

### REFERENCES


