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Background field removal for susceptibility mapping of human brain with large susceptibility variations

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Abstract

Purpose: In quantitative susceptibility mapping (QSM) of human brain, the background field induced by air-tissue interface varies significantly with respect to the rotation angle between the head and the static field, which may result in substantial error in the estimated magnetic susceptibility values. The goal of this study was to develop a strategy to better remove such orientation dependent background field.

Methods: An improved background field removal method is proposed based on the sophisticated harmonic artifact reduction for phase data using a region adaptive kernel (R-SHARP), named iRSHARP. It uses a spatially weighted spherical Gaussian kernel exploiting the amplitude, gradient, and wrap count of the phase map. The method was validated using both numerical simulations and in vivo human brain data at multiple head orientations. Performance was compared with the variable kernel (V-SHARP) and R-SHARP methods.

Results: The proposed iRSHARP method showed improved background removal over R-SHARP while cutting the computational time in half. As compared to V-SHARP and R-SHARP, the iRSHARP generated local field and susceptibility maps showed fewer artifacts in regions of large susceptibility variations, and for the in vivo human brain, the susceptibilities of the deep gray matter nuclei were consistent with the in vivo gold-standard “Calculation of Susceptibility through Multiple Orientation Sampling” (COSMOS) values.

Conclusion: iRSHARP can remove the orientation dependent background field effectively. Using iRSHARP, the paranasal sinus regions can be preserved in the brain mask and the brain integrity was conserved, which may facilitate further data analysis and clinical application.

Keywords

background field removal; orientation dependent; quantitative susceptibility mapping; spatially weighted kernel

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

1 | INTRODUCTION

Recent developments in quantitative susceptibility mapping (QSM) show its promise as a quantitative technique for MRI, especially in the diagnosis of neurodegenerative disorders that are related to brain iron changes,¹⁻⁵ for example, Alzheimer's disease,^{6,7} multiple sclerosis lesions,^{8,9} and Parkinson's disease.¹⁰⁻¹² QSM estimates the magnitude and spatial distribution of tissue susceptibility sources from the measured MRI phase or field map by solving an inverse problem, which provides significant anatomical details that cannot be observed in susceptibility-weighted magnitude maps.¹³⁻¹⁵ This is usually done by dipole inversion after removing the overwhelming background fields induced by static field inhomogeneities and dipole field sources outside the volume of interest (VOI), especially the air-tissue interfaces around the skull and various air cavities. These fields are superimposed onto the local field induced by brain tissue and may cause artifacts in QSM estimation if not sufficiently removed.¹⁶⁻¹⁸

A variety of strategies, such as the projection onto dipole field method,¹⁶ the sophisticated harmonic artifact reduction for phase data (SHARP) method,¹⁹ and some derived strategies,^{17,20-22} for example, the variable kernel SHARP method (V-SHARP)²³ and the regularization enabled SHARP method (RESHARP),²⁴ have been proposed to address this removal. Compared to the constant convolution kernel used in the original SHARP, the V-SHARP method uses an equally weighted spherical mean value (SMV) kernel of variable radius, which can better preserve the VOI boundary with less phase error, whereas RESHARP adds a Tikhonov regularization into the deconvolution that may suppress the residual background field with a large regularization parameter at a cost of possible oversmoothing of the local field. Given that the background field is generally much larger in the region of large susceptibility variations, for example, the mastoid cavity and the frontal, ethmoid, and paranasal sinuses,^{16,25} and extends into the adjacent brain tissues, the aforementioned methods are insufficient and need an eroded binary mask to exclude the sinuses and the contaminated tissues around the boundary regions, which is at the expense of losing coverage in those regions.

Recently, we proposed the background field removal method R-SHARP, which uses a region adaptive spherical Gaussian kernel (SGK) based on a fitting energy functional of the field map. R-SHARP could effectively suppress the susceptibility artifacts and compared favorably to V-SHARP to get an accurate estimation of the local field.²⁶ The R-SHARP method, however, consumes time to calculate the energy functional, in which there are also several regularization parameters to be optimized according to the field distribution. As we know, the background field in human brain MRI varies significantly with different head positions relative to the static field, especially around regions of large susceptibility variations. For the R-SHARP method, using the parameters of an energy functional optimized in the supine position, the background field could be well removed for the supine position, but errors remained in the estimated local fields at other head positions.

To address this, we redesigned the spatially weighted convolution kernel. Instead of fitting an energy functional, the amplitude and gradient of the phase map and phase wrap count are simply multiplied to control the spatial weight of the convolution kernel. This improved R-

SHARP (iRSHARP) approach therefore is more efficient in separating out the VOI into regions of large and minimal susceptibility variation using a predefined threshold. The proposed method is validated in a numerical simulation of 4 head positions and also applied to in vivo human brain data. To further evaluate the background field removal performance, single-orientation QSMs of human brain were reconstructed with the Structural Feature based Collaborative Reconstruction (SFCR) approach,¹⁸ and compared to quantitative susceptibility maps obtained by the COSMOS (Calculation of Susceptibility through Multiple Orientation Sampling), which is seen as the in vivo golden-standard reference.¹⁴ The experimental results demonstrated that the iRSHARP method could effectively remove the background field at different head positions, with less residual susceptibility artifacts in regions of large susceptibility, plus taking advantage of high computational efficiency.

2 | THEORY

2.1 | From SHARP to R-SHARP

In the SHARP method, the background field B_{ext} induced by susceptibility sources outside the VOI is assumed to be harmonic across the entire VOI and to satisfy the Laplace equation.^{19,27-29} Utilization of the SMV property can remove the background field and restore the local field from the total field perturbations for QSM, that is (Equation 1):

$$M(\delta - \rho_{SMV}) \otimes B^A(r) = M(\delta - \rho_{SMV}) \otimes B_{int}(r) \quad (1)$$

where M is a binary brain tissue mask defining the VOI and δ denotes the Dirac delta function. ρ_{SMV} is a nonnegative, radially symmetric, normalized SMV kernel. $B_{int}(r)$ is the local field induced by brain tissue susceptibility in VOI, and $B(r)$ is the total field perturbation with r denoting the dipole vector. The symbol $\otimes$ is the convolution operator. The equation shows that the selected convolution kernel directly affects the local field estimation. Several studies have discussed the selection of SMV radius to better eliminate the background field.^{20,21} Although a spatially variable Laplacian kernel with radius adapted to the frequency-offset-gradient magnitude reduced the artifacts in regions close to the cavities,³⁰ obvious artifacts still remain in the local field because of the SMV kernel.

In the vicinity of air-tissue boundaries (e.g., skull and paranasal sinuses), where large susceptibility variations exist, the background fields are so large that an SMV kernel with either fixed or varying radius is insufficient to eliminate them, resulting in residual error in the estimated local field.²⁶ These regions often need to be excluded by brain mask erosion at the expense of losing information about local fields and thus susceptibility measures in these regions. The R-SHARP method takes advantage of the energy functional to separate the VOI into subregions of either sufficient homogeneity or large susceptibility variations, adopting normalized SMV and SGK, respectively. The spatially weighted SGK is calculated from the 3D Gaussian probability distribution function and formulated as Equation (2):

$$\rho_{\text{SGK}}(x, y, z) = \frac{1}{\sqrt{2\pi}\sigma(\mathbf{r})} \exp\left(-\frac{x^2 + y^2 + z^2}{2\sigma^2(\mathbf{r})}\right) \quad (2)$$

where (x, y, z) denote the coordinates of points in the SGK. Determined by its standard deviation $\sigma(\mathbf{r})$, an SGK of smaller σ has larger central weight. Replacing ρ_{SMV} with ρ_{SGK} in Equation (1), with a suitable σ for the SGK at each voxel, the method can have a good performance in estimating the local field in large susceptibility regions, even when the whole paranasal sinus regions are preserved in the brain mask.

To evaluate the impact of σ value on the background field removal, we used a set of uniform SGKs of different values of σ that are 3.0, 1.6, 1.0, and 0.2 for each estimation as shown in Figure 1d to 1g. As the σ value decreases (from Figure 1d to 1g), the residual background field becomes smaller and gradually disappears. Although a small σ may suppress the residual error better, a uniform value for the whole volume in the brain may cause part of the local field to be removed as well, as denoted by the arrow in Figure 1g. Hence, the background field should be removed with a voxel-wise region adaptive kernel, that is, a convolution kernel of small σ is applied to the strong background field and vice versa.

2.2 | Background field removal with iRSHARP

The phase map acquired with the gradient echo sequence in MRI results from the evolution of total field perturbations under the TE .¹⁹ However, the raw phase is mathematically wrapped into the interval $(-\pi, \pi]$ and a Laplacian phase unwrapping technique is usually used to obtain the unwrapped phase $\varphi_{\text{un}}(r)$.³¹ Then, the measured phase can be formulated into Equation (3):

$$\varphi_{\text{un}}(\mathbf{r}) = \varphi_{\text{TE}}(\mathbf{r}) - \varphi_0(\mathbf{r}) = -\gamma TE \cdot B^{\Delta}(\mathbf{r}) - 2\pi TE \cdot \Delta f_{\text{ref}} \quad (3)$$

where γ is the gyromagnetic ratio and $\varphi_{\text{TE}}(r)$ is the phase measured at echo time TE and $\varphi_0(r)$ the initial phase distribution at $TE = 0$ ms. f_{ref} is the frequency difference between the Larmor frequency f_0 and the adjusted reference frequency f_{ref} of the MR system, which is a homogeneous constant offset and can be neglected here.¹⁹

The total induced perturbations $B^{\Delta}(\mathbf{r})$ under the static field B_0 are described by a convolution of the magnetic susceptibility $\chi(\mathbf{r})$ with the z-component $d_z(\mathbf{r})$ of the spatial unit dipole¹⁹ (Equation 4):

$$B^{\Delta}(\mathbf{r}) = |B_0| \cdot \int \chi(\mathbf{r}') \cdot d_z(\mathbf{r} - \mathbf{r}') d^3\mathbf{r}' \quad (4)$$

where $d_z(\mathbf{r})$ is defined as Equation (5):

$$d_z(r) = \frac{3 \cdot \cos^2 \theta - 1}{4\pi |\mathbf{r}|^3} \quad (5)$$

in which θ is the angle between $\mathbf{r}$ and B_0 . Because θ affects the field distribution, the background field varies with the head rotation angle and noticeable differences can be observed such as around the paranasal sinuses in Figure 1b and 1c, especially an asymmetry between left and right hemispheres in the head position of tilting to right and left, respectively.

As we know, the regions of large susceptibility variation correspond to large phase gradients. In iRSHARP, the field gradient is used to adjust the spatial weight of SGK as Equation (6):

$$\sigma(\mathbf{r}) = \frac{1}{C \cdot (\nabla \varphi_{\text{un}}(\mathbf{r}) + \varepsilon)} \quad (6)$$

where the adjustable parameter C is a positive constant and ∇ denotes the gradient operator. ε is a positive constant to avoid dividing by 0 and set to be 1. However, doing this, some residual error is still observed in regions with a strong background field in Figure 2g, because the phase gradient in the central region around the paranasal sinus may be small as shown in the zooming view in Figure 2d. Therefore, the phase amplitude should also be taken into account as Equation (7):

$$\sigma(\mathbf{r}) = \frac{1}{C \cdot (\nabla \varphi_{\text{un}}(\mathbf{r}) + \varepsilon) \cdot (\varphi_{\text{un}}(\mathbf{r}) + \varepsilon)} \quad (7)$$

Compared to the single gradient of phase, the multiplication between the phase amplitude and its gradient has better performance in separating the large susceptibility regions from homogeneous regions. Especially, introducing the phase amplitude into the $\sigma(\mathbf{r})$ definition can address the background removal in the region of strong background field with small phase gradient. However, the small residual error in Figure 2h indicates that this spatial weight is still not sufficient to achieve an excellent background field removal.

Defining the nonlinear wrapping operator $W[\bullet]$, the relationship between the unwrapped phase $\varphi_{\text{un}}(\mathbf{r})$ and the wrapped phase φ_w can be represented³² by $\varphi_w(\mathbf{r}) = W[\varphi_{\text{un}}(\mathbf{r})] = W[-\gamma \text{TE} \cdot B(\mathbf{r})]$, where the wrap count at each voxel can be calculated from Equation (8):

$$K(\mathbf{r}) = (\varphi_{\text{un}}(\mathbf{r}) - \varphi_w(\mathbf{r})) / 2\pi \quad (8)$$

We observe that $K(\mathbf{r})$ is related to $B(\mathbf{r})$ and presents strong contrast as shown in Figure 2c. Thus, the wrap count is normalized into the scale of [0, 1] through dividing by the maximum and then added into the design of the spatial weighting factor (Equation (9):

$$\sigma(r) = \frac{1}{C \cdot (\nabla \varphi_{\text{un}}(r) + \varepsilon) \cdot (\varphi_{\text{un}}(r) + \varepsilon) \cdot (\mathbf{K}(r) + \varepsilon)} \quad (9)$$

The adjustment constant C is determined by parameter sweeping in the Results section. Using Equation (9), we define $\hat{\sigma}(r) = \frac{1}{\sigma(r)} = C \cdot (\nabla \varphi_{\text{un}}(r) + \varepsilon) \cdot (\varphi_{\text{un}}(r) + \varepsilon) \cdot (\mathbf{K}(r) + \varepsilon)$. As shown in Figure 2f, the phase map can be separated into 2 subdomains with large susceptibility variation D_1 and good susceptibility homogeneity D_2 using a threshold related to $\hat{\sigma}(r)$. Taking $\bar{\sigma}$ and σ_{max} to denote the average and maximum values of $\hat{\sigma}(r)$, the simple threshold $\bar{\sigma}$ may not be robust to different susceptibility distributions in multiple-orientation imaging. Here, we design a function as $(\sigma_{\text{max}} - \bar{\sigma}) / (\sigma_{\text{max}} + \bar{\sigma})$ which has the range of 0 to 1, and increases monotonically with the ratio $\sigma_{\text{max}} / \bar{\sigma}$, that is, the function value gets close to 1 as the ratio $\sigma_{\text{max}} / \bar{\sigma}$ increases. In this case, the threshold calculated by $\hat{\sigma}_0 = \bar{\sigma} + (\sigma_{\text{max}} - \bar{\sigma}) / (\sigma_{\text{max}} + \bar{\sigma})$ is more sensitive to the σ_{max} that is determined by the maximum of $(\nabla \varphi_{\text{un}}(r) + \varepsilon) \cdot (\varphi_{\text{un}}(r) + \varepsilon) \cdot (\mathbf{K}(r) + \varepsilon)$. Then, the spatial weighting factor $\sigma(r)$ is exploited to reformulate the convolution kernel ρ_{SGK} in Equation (2).

Because the voxels in the homogeneous subdomain have large standard deviations, the spatial weights in SGK are approximately equal. In this case, the Gaussian convolution kernel applied in the homogeneous subdomain can be substituted into the SMV kernel ρ_{SMV} . Hence, our proposed background field removal algorithm iRSHARP becomes Equation (10):

$$\mathbf{B}_{\text{temp}}^{\Delta}(r) = \begin{cases} (\delta - \rho_{\text{SGK}}) \otimes \mathbf{B}_{\text{int}}(r), & r \in D_1 = \{\hat{\sigma}(r) > \hat{\sigma}_0\} \\ (\delta - \rho_{\text{SMV}}) \otimes \mathbf{B}_{\text{int}}(r), & r \in D_2 = \{\hat{\sigma}(r) \leq \hat{\sigma}_0\} \end{cases} \quad (10)$$

where $\mathbf{B}_{\text{temp}}^{\Delta}$ is the interim variable data and the local field can be calculated by the inverse convolution in Fourier space. The radius of the kernel is initialized to be 6 voxels and decreases to 1 as the moving voxel approaches the boundary of the VOI, similar to the R-SHARP method.²⁶ In Figure 2g to 2i, the residual background is better suppressed with the spatial weight combining the gradient, amplitude, and wrap count of phase map than merely the gradient and the phase itself.

3 | METHODS

The proposed method was validated both on a multiple-orientation numerical phantom and in vivo human brain data. The results were compared with the V-SHARP and R-SHARP methods.^{23,26} Root mean square error (RMSE) was used to quantitatively evaluate the result accuracy in numerical simulations. Because there is no ground truth of local field for in vivo human brain, we evaluate the success of background field removal in 2 different ways. It has been demonstrated that the R-SHARP method outperforms the previous methods in preserving the integrity of the brain tissue in regions around large susceptibility variations,²⁶

so we took it as the main comparison method to evaluate the results for those areas. On the other hand, we used the local field estimation of the RESHARP method to evaluate the performance in the other tissue structures, with the vicinity of air-tissue boundary excluded by brain mask erosion. The single-orientation QSM human brain was reconstructed by the SFCR method utilizing the COSMOS result as the gold-standard reference. All implementations were performed using Matlab 2013a (The MathWorks, Inc., Natick, MA), on a personal computer with Intel (R) Core™ i7-4790 CPU, 8GB RAM. The code of our iRSHARP method is available on the website: <http://www.mri-resource.kennedykrieger.org/software>.

3.1 | Numerical simulation

A numerical human brain (VOI) was created in a $160 \times 160 \times 80$ matrix at $1 \times 1 \times 1 \text{ mm}^3$ isotropic resolution, in which 5 small structures were embedded to mimic caudate nucleus (CN), substantia nigra (SN), globus pallidus (GP), vein, and paranasal sinus, and another structure was created outside the VOI to simulate an air cavity. The susceptibilities of these structures were set to 0.05, 0.16, 0.1, 0.3, and 9.4 parts per million (ppm), respectively, whereas those of the remaining regions in the brain were set to 0 ppm as shown in Figure 3. In addition, 0-mean Gaussian white noise with unity standard deviation was added to both the real and imaginary parts of the complex data. The simulated main field B_0 was 7.0T and $TE = 10$ ms. To simulate different head positions, we varied the brain at supine position to right orientations (12° , 20° , and -12°), left (15° , -20° , and 25°), and back (-4° , 6° , and -12°) as shown in Figure 3. The FSL FLIRT tool was used to coregister the nonsupine positions to the supine position, and then the total fields were obtained by utilizing a forward calculation.^{19,33} The local fields were calculated in the same way with the absence of paranasal sinuses and Gaussian noise, whereas the simulated background field was achieved by subtracting the local field from the total field. A binary mask was exploited to extract the brain tissue from the paranasal sinuses and background regions. The C value of R-SHARP was optimized by the parameter-sweeping method varying from 1.0 to 10.0 in the step of 0.5, and set to be 8.0.²⁶ The threshold of truncated singular value decomposition (TSVD) was 0.05, and the radius of SGK varied from 6 voxels to 1 for V-SHARP, R-SHARP, and iRSHARP.

3.2 | In vivo human brain imaging

The experiment was approved by the local Institutional Review Board. It was performed on a healthy male volunteer at the F.M. Kirby Research Center in Kennedy Krieger Institute and Johns Hopkins University using a multiecho gradient recalled echo pulse sequence on a 7T MRI scanner (Philips Healthcare, Best, The Netherlands) with a 32-channel Novamedical head coil. The matrix size was $224 \times 224 \times 110$, field of view $220 \times 220 \times 110 \text{ mm}^3$, 8 echoes, $TR/TE_1 \text{ TE} = 45/2/2$ ms, and total scanning time 5:15 minutes. The subject was scanned with his head placed at 4 different head positions. The rotation angle for each tilting position varied from 5 to 22° from the axis of the static magnetic field B_0 .

The FSL FLIRT tool was used to match the first echo magnitude data of the 3 tilting positions into that of the supine position to obtain the coregistration transformation matrices, which were then applied to coregister the magnitude and phase data acquired at each echo

time.^{26,34} The Laplacian phase unwrapping method was applied to remove the phase wraps, and linear fitting over echo time was then used to generate the frequency map.³⁴ A brain mask was generated using the FSL BET tool, applied to the magnitude image of the supine position, with regions around air-tissue interface with large susceptibility variation preserved as well. The regions of interest of deep gray matter were extracted based on QSM human brain atlas for 3D data using the software Large Deformation Diffeomorphic Metric Mapping (LDDMM).³⁵

In the COSMOS method, the background field was removed by the RESHARP method with an eroded binary mask to maximally reduce the influence of large susceptibility variations, because RESHARP using a smooth function can effectively mitigate the background field in the homogeneous regions.²⁴ The regularization parameter of RESHARP was optimized as 0.01 with a convolution kernel of radius 6, and the susceptibility maps were estimated using LSQR solver with a relative convergence tolerance of 10^{-5} . The C value of R-SHARP was optimized to be 1.8 in the same way, and the threshold for TSVD was 0.10 for V-SHARP, R-SHARP, and iRSHARP.

4 | RESULTS

4.1 | Numerical simulation

In the iRSHARP method, the value of constant C is determined using the data at the supine position assuming that it is not affected by the orientation variations. It is swept from 0.01 to 1.36 with step size 0.05 plotted against RMSE in Figure 4a, in which the RMSE reduces with increasing C value, leveling off at higher C . Meanwhile, susceptibility artifacts around the simulated sinuses are better suppressed with greater values of C as shown in Figure 4b to 4d. Hence, we set C to be 0.8 in the simulation experiment. Figure 4e to 4h shows the estimated local field maps of numerical simulations using V-SHARP, R-SHARP, and iRSHARP at 4 orientations. We see that there are obvious residual errors in the results of the V-SHARP method. The R-SHARP method removes the background well at most positions, but very small orientation-dependent residual errors can be observed at the boundary of high susceptibility regions as shown in the zoomed views in Figure 4. In contrast, the iRSHARP method substantially removes the background field and restores the local field from the total field at all positions. The histograms of the phase-difference maps relative to the ground truth are shown in Figure 5, which further demonstrates that the iRSHARP method achieves more accurate estimations than the other methods in multiple orientations. The difference range in the histograms of V-SHARP is approximately $(-100, 100)$ at all head positions, confirming significantly larger residual errors than the other 2 methods. For the supine position, the histograms of the R-SHARP and iRSHARP methods present comparable statistical errors. However, at the other positions, the errors of iRSHARP are mostly in the range of $(-5, 5)$, whereas those of R-SHARP range from $(-10, 10)$.

Table 1 compares the RMSE values of the estimated local fields and the computation time of the 3 methods. The iRSHARP method has the best RMSE for all orientations, that is, the estimated local field maps are closest to the simulated local field as compared to those from R-SHARP and V-SHARP. Moreover, the computational time of iRSHARP method was less than half of that for the R-SHARP method.

4.2 | In vivo human brain

The C value for the in vivo human brain data was optimized in a way similar to the numerical simulation, sweeping from 0.01 to 0.40, but now with step size 0.01. A small C value of 0.01 will cause serious residual phase error at all head positions as shown in the first row of Figure 6b, but a large value of $C = 0.40$ may lead to removal of part of the local field, especially around the sinus region. In the range of 0.20 to 0.30, there was very small residual error and brain tissues could be well distinguished. Hence, $C = 0.25$ was selected as the optimal value for all orientations. The computation times were around 85.73, 323.4, and 137.8 seconds for V-SHARP, R-SHARP, and iRSHARP methods, respectively.

Figure 7 shows the background field removal of the 3 methods as well as the corresponding difference maps of V-SHARP and iRSHARP with respect to the R-SHARP method. In Figure 7a to 7c, the estimated local fields are shown for the in vivo human brain at different head positions. It is clear that the results of the iRSHARP method have a high similarity with that of the R-SHARP method, whereas the residual phase error in the V-SHARP method is stronger than the other 2 methods as denoted by the orange arrows, as well as illustrated in the difference map in Figure 7e. We can see that the V-SHARP method cannot remove the background field effectively and noticeable orientation dependent errors remain. The R-SHARP method performs well at the supine position, but small residual errors can still be observed at the other head positions as denoted by the orange arrows. The results of the iRSHARP method have the best performance at all head orientations with much reduced error.

Figure 8 shows profile comparisons along the orange lines in Figure 8a (local field maps estimated by RESHARP with the vicinity of air-tissue boundary excluded by brain mask erosion). The 4 methods present similar variation trends at the supine position. Whereas the results of the iRSHARP and R-SHARP methods are close to the RESHARP for all head positions, those of V-SHARP are different in several boundary regions for the 3 nonsupine positions.

Residual background fields usually yield significant shadow artifacts in QSM reconstructions. Figure 9 shows single-orientation susceptibility maps reconstructed by the SFCR method with different local field estimations to further demonstrate the performances for the different background field removal approaches. Besides regions around the VOI boundary, there were obvious artifacts over regions with large susceptibility variations when using local field estimates from V-SHARP at the supine position. As the head tilted to other positions, the orientation-dependent residual phase errors caused serious artifacts, as denoted by the arrows in Figure 9a. Given that the iRSHARP and R-SHARP methods give quite similar local field estimation for the supine position, it is not unexpected that comparable susceptibility maps were also obtained. However, for the other head positions, small artifacts appeared around the sinus regions in the R-SHARP method that were reduced in the result of the iRSHARP method.

Mean susceptibilities of 5 nuclei in deep gray matter were calculated from the 3 methods at 4 head positions and compared to the in vivo gold-standard reference values of COSMOS in Figure 9b to 9c. Although all values are comparable within experimental error, there are

some trends. As we know, the values of GP, RN (red nucleus), and SN are more sensitive to the head orientation than those of CN and PU (putamen).¹⁸ Moreover, SN and RN are closer to the sinus where residual phase errors may remain in the local field estimation. As a consequence, the susceptibilities of GP, RN, and SN estimated from V-SHARP are larger than those determined from R-SHARP and iRSHARP. The significant orientation dependent artifacts in the V-SHARP method give rise to the biggest deviation of RN and SN from the COSMOS reference in the supine position, but, on the other hand, the R-SHARP approaches deviate more for the other directions for these structures. Because CN and PU are farther from the sinus, comparable estimations were found as illustrated in Figure 9c.

5 | DISCUSSION AND CONCLUSIONS

We evaluated a new background field removal method called iRSHARP and validated its feasibility using numerical simulations and in vivo human brain data acquired at multiple head orientations. Both the visually assessed image quality and quantitative analyses in the phantom demonstrated that the iRSHARP method was superior to the compared methods in background field removal, especially for regions around large susceptibility variation regions.

For in vivo human MRI, the field perturbations are related to the angle between the head position and the static field B_0 . When the head is in tilted positions, artifacts induced by large susceptibility variations also present significant orientation dependence in the estimated local field as shown in Figure 6. The V-SHARP method uses the SMV kernel and can successfully remove the background field when regions of large susceptibility variations are excluded by a binary mask.¹⁶ Nevertheless, once these regions are taken into account, the background field removal is incomplete, partly because some nonharmonic components that cannot be removed by the property of SMV. Although the R-SHARP method enables detection of the field inhomogeneity degree with the value of the energy functional, some regularization parameters used in the energy fitting functional need to be adjusted according to the phase map. This determination is time-consuming, which limits the algorithm's applicability.

In the iRSHARP approach, similar to R-SHARP, regions of large susceptibility variation and susceptibility homogeneity are separated out and evaluated differently based on the phase information. However, this is done in a simpler and better way that uses the multiplication of the phase amplitude, its gradient, and the phase wrap count. The phase amplitude and its gradient can directly reflect the phase variation, whether caused by tissue susceptibility or the air-tissue interface. Combination with the phase wrap count, which is approximately proportional to the phase amplitude, may further enhance the contrast of $\text{map}\hat{\sigma}(r)$. Then, the standard deviation of the voxel-wise adaptive SGK is designed relative to this product. Hence, the spatial weight of the convolution kernel applied to the background removal in the air-cavity region has high value at the kernel center and decays rapidly to near-0 values for adjacent weights. However, in regions of homogeneous tissues, the spatial weight at each kernel point is almost equal and an SMV may be used instead. The iRSHARP method has only 1 adjustable constant C . Hence, it can perform background field removal with higher computational efficiency than R-SHARP, namely more than twice as fast. On the other hand,

the value of C is determined by the phase map contrast in the VOI. In the numerical simulations, the contrast between the large susceptibility variations and homogenous tissues was significantly stronger than that of the in vivo human brain. Thus, C was set to be 0.8 for the numerical simulations and only to 0.25 for the in vivo data.

In this paper, we use isotropic voxel sizes in both numerical simulations and in vivo human brain data. However, anisotropic voxel size, especially relative to B_0 orientation, may be acquired in practical imaging with large slice thickness. Researchers have demonstrated the effect of the imaging resolution on the sphere kernel radius and the TSVD regularization value in the original V-SHARP method, and they propose to define the radius of the sphere kernel in millimeters in order to make the background correction independent of imaging and processing resolution.³⁶ In a similar way, the SGK radii in our proposed iRSHARP method are equal to the physical radii divided by the voxel size, in which voxel size asymmetry is also taken into account. Besides, sweeping C from 0.01 to 0.81 with step 0.05 in the simulation experiment, we observe that the residual error in the estimated local field will become larger with the voxel size increasing from (1, 1, 1) to (1, 1, 3). However, the RMSE curves of different imaging resolutions can converge at similar values of C , which means that the voxel size asymmetry has no significant effect on the parameter optimization in iRSHARP method. More illustrations are in the Supporting Information Figures S1 and S2.

Unfortunately, a quantitative comparison of estimated local fields cannot be done for in vivo data because of the lack of a ground truth. Thus, we evaluated the results in 2 ways, with the whole paranasal sinus region either preserved or excluded in the brain mask. The RESHARP method was added into the comparison with brain mask erosion based on its good performance for the background field removal in homogeneous field regions. The experimental results on local field estimations and susceptibility reconstruction demonstrated that under both conditions, that is, with or without the sinus region included in the brain mask, the iRSHARP method achieved comparable results to R-SHARP in the numerical simulations as well as the human brain data, and these results were not affected by different head orientations.

Given that the proposed iRSHARP method can effectively remove the background field while preserving the brain tissue integrity and suppressing susceptibility artifacts especially in regions of large susceptibility variations, we believe it will facilitate background field removal in applications in tissues with large susceptibility variations and orientation variations, for example, those around the sinus in human brain, organs with metal implants, etc.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Illustration of the influence of head rotation on the background field and impact of σ on the background field removal at supine position. (a–c) Background fields at different head positions: (a) supine position, (b) tilting to right, and (c) tilting to left. The background field varies with the head positions around the paranasal sinuses as denoted by the arrows. (d–g) Results of background field removal with uniform σ value: (d) $\sigma = 3.0$, (e) $\sigma = 1.6$, (f) $\sigma = 1.0$, and (g) $\sigma = 0.2$. As the σ value decreases, the residual background field in the rectangles becomes smaller and gradually disappears

FIGURE 2.

Comparison of the results using different ways to construct SGK. (a) Raw phase map $\phi_w \in [-\pi, \pi]$, (b) unwrapped phase map, (c) map of wrap count, (d) phase gradient map with local zooming, (e) multiplication of phase gradient and unwrapped phase, (f) $\hat{\sigma}$ map noted with 2 subdomains of D_1 and D_2 , and (g–i) local field estimation using (d–f), respectively, where arrows point out the residual background field

FIGURE 3.

Numerical simulation of multiple head positions. (a–d) Simulated maps of susceptibility, total field, and local field at different orientations. The susceptibility maps of the tilting positions were coregistered to the supine position and then the total fields and local fields were calculated

FIGURE 4.

C optimization in numerical simulation and the results on background field removal. (a) Parameter sweeping curve, where the RMSE reduces with increasing *C* value and levels off at higher values, (b–d) the results with different *C* values, *C* = 0.01, 0.4, and 0.8, respectively, and (e–h) the estimated local fields by V-SHARP, R-SHARP, and iRSHARP at different head orientations with small orientation-dependent residual errors shown in the zoomed views

FIGURE 5.

Comparison of the phase-difference maps and their histograms for the 3 methods relative to the ground-truth phase. The difference histograms of V-SHARP show a significantly larger range than iRSHARP and R-SHARP, whereas iRSHARP exhibits a comparable result to R-SHARP at the supine position, but more accurate estimations than R-SHARP at the tilted positions. The difference maps are shown in the scale of $(-20, 20)$ Hz

FIGURE 6.

Optimization of C value for in vivo human brain. (a) Phase map and (b) local field estimations with different C values, $C = 0.01$, 0.25 , and 1.40 , respectively. The degrees of the head rotation are supine $(-0.89, 2.08, -4.19)$, right $(-13.76, -0.83, -6.64)$, left $(11.51, 21.83, -12.95)$, and back $(-3.72, 5.92, -12.81)$

FIGURE 7.

Comparison on estimated local fields in the region of large susceptibility variations. (a–c) Local fields calculated by V-SHARP, R-SHARP, and iRSHARP, respectively, where noticeable orientation-dependent errors can be observed as denoted by the orange arrows. (d) The difference maps between (a) and (b), and (e) the difference maps between (c) and (b)

FIGURE 8.

Comparison on background field removal with RESHARP in the homogeneous regions. (a) Local field estimated by RESHARP and (b) profiles of the orange lines in (a)

FIGURE 9.

Comparison of susceptibility maps (23rd) with background field preprocessed by different methods. (a) Susceptibility maps of different head positions reconstructed with background field removed by V-SHARP, R-SHARP and iRSHARP, respectively with arrows marking out the region of different artifact levels. (b) susceptibility maps reconstructed by COSMOS with background field removed by RESHARP, (c) susceptibilities of CN, PU (putamen), RN (red nucleus), GP, SN at different head positions

TABLE 1

Estimated local field RMSE (Hz) and computation time

Method	Supine	Right	Left	Back	Time(s)
V-SHARP	34.114	41.956	25.083	24.449	34.8
R-SHARP	2.805	2.770	2.988	2.780	122.1
iRSHARP	1.763	1.528	1.545	1.800	58.9