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Automated Adaptive Preconditioner for Quantitative Susceptibility Mapping

Zhe Liu^{1,2}, Yan Wen^{1,2}, Pascal Spincemille², Shun Zhang^{2,3}, Yihao Yao^{2,3}, Thanh Nguyen², Yi Wang^{1,2,*}

¹Department of Biomedical Engineering, Cornell University, Ithaca, New York, USA

²Department of Radiology, Weill Cornell Medical College, New York, New York, USA

³Department of Radiology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Abstract

Purpose: To develop an automated adaptive preconditioner for QSM reconstruction with improved susceptibility quantification accuracy and increased image quality.

Theory and Methods: The total field was used to rapidly produce an approximate susceptibility map, which was then averaged and trended over R2* binning to generate a spatially-varying distribution of preconditioning values. This automated adaptive preconditioner was used to reconstruct QSM via total field inversion and compared with its empirical counterparts in a numerical simulation, a brain experiment with 5 healthy subjects and 5 patients with intracerebral hemorrhage, and a cardiac experiment with 3 healthy subjects.

Results: Among evaluated preconditioners, the automated adaptive preconditioner achieved the fastest convergence in reducing the root-mean-square-error of the QSM in the simulation, suppressed hemorrhage-associated artifacts while preserving surrounding brain tissue contrasts, and provided cardiac chamber oxygenation values consistent with those reported in the literature.

Conclusion: An automated adaptive preconditioner allows high quality QSM from the total field in imaging various anatomies with dynamic susceptibility ranges.

Keywords

QSM; total field inversion; preconditioning; cardiac; hemorrhage

INTRODUCTION

Quantitative Susceptibility Mapping (QSM)(1) has been an increasingly active field in MRI to a study tissue's magnetic susceptibility property, as summarized in recent review articles from many leading groups (2–14). Susceptibility changes in many pathological processes, including neurodegeneration, inflammation, hemorrhage, oxygenation, and calcification (15). QSM has been demonstrated as a powerful tool for multiple sclerosis lesion

*Correspondence to: Yi Wang, Ph.D., 515 East 71st St, Suite 102, New York, NY, 10021. yiwang@med.cornell.edu.

characterization (16,17), mapping iron overload in Parkinson's disease (18) and Alzheimer's disease (19–21), monitoring cerebral cavernous malformation (22), measuring oxygenation (23,24), assessing brain tumor (25–28), and guiding surgery for deep brain stimulation (29). A fundamental approach in reconstructing the tissue susceptibility distribution from the measured magnetic field is to optimally solve the ill-posed field-to-susceptibility inverse problem with additional structural knowledge using Bayesian inference (7). Current numerical optimization solvers are iterative, and it is desired to accelerate iteration convergence for targeted accuracy. These iterative solvers use a universal stopping criterion regardless of the image content, and iteration may be stopped before adequate convergence for lesions with large susceptibility values that occupy small fractions of the image volume, promoting severe streaking artifacts.

Preconditioning has been proposed to accelerate iteration convergence in QSM (30). Preconditioned QSM can reconstruct QSM of the entire image volume (including bone and air cavities) directly from the total field without explicit or implicit background field removal. By incorporating R2* information in the preconditioner, preconditioned QSM can reduce hypointense artifacts associated with intracerebral hemorrhage (ICH) which has very high susceptibility values. However, the reported preconditioner consists of a simple binary image with dual values selected manually for a given anatomy or application.

In this work, we propose a general and automated framework for constructing an adaptive preconditioner for the total field and R2* derived from the input gradient echo data, without assumptions on the underlying image content or the need for a manual selection of preconditioning weights. The automated adaptive preconditioner is compared with its empirical counterpart (30) by their reconstruction performance in TFI across different imaging scenarios including healthy brain, ICH, and cardiac MRI.

THEORY

A distribution of spatially varying susceptibility sources perturbs the external applied magnetic field B_0 . The exact relation by which tissue susceptibility determines the field perturbation can be derived using Maxwell's equations (31–33) and the Lorentz sphere correction model (34,35), resulting in the following convolutional form:

$$\frac{b}{B_0} = d * \chi \quad [1]$$

where b is the observed perturbation field by the tissue and d is the dipole kernel used in the convolution operation $*$, which can be regarded as the magnetic field perturbed by a unit point susceptibility source (36). If the MR images are acquired using a gradient echo sequence, the complex MRI signal, after de-modulation of the spatial encoding gradient field, reflects the perturbed magnetic field in a linear fashion via its phase component:

$$I = me^{-R2^*TE} e^{-i2\pi f B_0 TE} + n \quad [2]$$

where $f = b/B_0$ is the normalized total field perturbation, m is the magnitude of the magnetization damped with an exponential $R2^*$ decay, TE is the acquisition time for the corresponding gradient echo, n is random noise, and I is the acquired complex MRI signal. Eq. 2 is typically used to estimate the field perturbation through least-square fitting across different echo time TEs:

$$f = \operatorname{argmin}_b \sum_{j=1}^{N_{TE}} \left\| I_j - |I_j| e^{i2\pi f B_0 TE_j} \right\|_2^2 \quad [3]$$

Given the total field estimation f , the inversion process for solving χ in Eq. 1 is still non-trivial, due to the ill-posedness in the dipole kernel d (36). Accordingly, an optimization framework is employed which preserves fidelity in Eq. 1 and imposes regularization to counter its ill-posed nature. Based on the previous work of total field inversion (TFI) (30) and QSM with automatic zero-referencing (37), we propose the following optimization framework for QSM:

$$\hat{\chi} = P\hat{y}, \hat{y} = \operatorname{argmin}_y \frac{1}{2} \|w(f - d * Py)\|_2^2 + \lambda_1 \|M_G \nabla Py\|_1 + \lambda_2 \left\| M_2 \left(Py - \overline{(Py)}_{M_2} \right) \right\|_2^2 \quad [4]$$

with χ the susceptibility map over the entire field of view, $*$ the convolution with the dipole kernel d , w the noise weighting, f the total field, ∇ the gradient operator and M_G the binary edge mask derived from the magnitude image (38). The optimal solution for intermediate variable $\hat{y}$ is multiplied with the preconditioner P to recover the final susceptibility map $\hat{\chi}$. In the last term, the L_2 regularization enforces homogeneity within a pre-determined binary mask M_2 , which is equal to 1 where homogeneity is expected. For example, M_2 can be the ventricular cerebrospinal fluid (CSF) in brain QSM. $\overline{(\cdot)}_{M_2}$ denotes the operator that computes the mean value within M_2 . P is the preconditioner constructed as a binary matrix in (30):

$$P(\mathbf{r}) = \begin{cases} 1, & \mathbf{r} \in M \\ P_S, & \text{otherwise} \end{cases} \quad [5]$$

where $\mathbf{r}$ denotes the location for each voxel, M is the mask for tissue ROI. $P_S > 1$ is empirically determined for each anatomy and application. As a search step size in numerical optimization, the preconditioner is always positive. Given the availability of $R2^*$ information, P can be constructed as:

$$P(\mathbf{r}) = \begin{cases} 1, & \mathbf{r} \in M \cap M_{R2^*} \\ P_S, & \text{otherwise} \end{cases} \quad [6]$$

where M_{R2^*} is a region with low $R2^*$ value ($M_{R2^*}: = R2^* < 30 \text{ s}^{-1}$) (30). The difference in those weights (1 vs. P_S) represents the contrast between weak susceptibility of soft tissues and relatively strong susceptibility sources including air, bone and hemorrhage.

To fully exploit the capacity of preconditioning in accelerating reconstruction of QSM of various anatomies, P needs to be extended from binary values to a continuous range of weights. We propose automated generation of an adaptive preconditioner from the total field f and $R2^*$, as illustrated in Figure 1. First, an approximate susceptibility map is estimated rapidly from the field input f . The susceptibility of strong sources outside the region of interest (ROI) M is estimated using the projection onto dipole fields method (PDF) (39), while the susceptibility inside M is calculated using the Laplacian boundary values method (LBV) (40) followed by Truncated K-space Division (TKD) (41). These two susceptibility components are combined into a single map χ_{est} .

Then, weights of the preconditioner are generated from χ_{est} by addressing noise and artifacts in χ_{est} in the following manner of averaging and trending. We group voxels with similar spatial or $R2^*$ properties, depending on where the voxels are relative to the ROI M , and calculate the median χ^{med} of absolute susceptibility values within each group. Inside M , voxels are grouped by their $R2^*$ values $\mathcal{R}$, each group is defined by a bin of 1-s^{-1} width in $R2^*$ value, and χ^{med} is determined by fitting $|\chi_{\text{est}}|$ to a sigmoid curve with respect to $\mathcal{R}$:

$$\chi^{\text{med}} \sim (\sigma_2 - \sigma_1) \frac{1}{1 + e^{-\frac{(\mathcal{R} - s_1)}{s_2}}} + \sigma_1. \quad [7]$$

Here $[\sigma_1, \sigma_2]$ control the output range and (s_1, s_2) control the shape. The choices of $R2^*$ binning and sigmoid curve are motivated by connections between $R2^*$ and susceptibility, and by soft thresholding.

Outside M , due to the absence of reliable $R2^*$ measurement, voxels are grouped by their distance $\mathcal{D}$ towards the boundary of the mask M . Each group is denoted by a bin of 1-mm width in $\mathcal{D}$ value, and χ^{med} is calculated by fitting $|\chi_{\text{est}}|$ to a cubic decay function with respect to $\mathcal{D}$:

$$\chi^{\text{med}} \sim \sigma_0 \left(1 + \frac{\mathcal{D}}{r_0}\right)^{-3} \quad [8]$$

where σ_1 and r_0 control its scale and decay rate, respectively. The cubic decay is motivated by a similar spatial decay of the dipole kernel (for a numerical explanation, see Supporting Information: cubic decay in PDF estimated susceptibility distribution).

The final preconditioner P is then constructed as:

$$P(\mathbf{r}) = \begin{cases} \frac{\sigma_0}{\sigma_1} \left(1 + \frac{\mathcal{D}}{r_0}\right)^{-3}, & \mathbf{r} \notin M \\ \left(\frac{\sigma_2}{\sigma_1} - 1\right) \frac{1}{1 + e^{-\left(\mathcal{R} - s_1\right)/s_2}} + 1, & \mathbf{r} \in M \end{cases} \quad [9]$$

Note that, consistent with previous work (30), we scale P by σ_1 such that the weight for soft tissues (low R_2^*) is close to 1. The generated preconditioner P is provided to TFI (Eq. 4), which is solved using the Gauss Newton method combined with the conjugate gradient (CG) solver (30,42).

METHODS

We designed a numerical simulation to analyze the accuracy of the proposed automated preconditioner P_{auto} (Eq. 9) for healthy brain (non-ICH) and brain with ICH, compared with its empirical counterparts P_{emp} (Eq. 5) and $P_{\text{emp}+R_2^*}$ (Eq. 6). We then compare their performance for in vivo brain QSM of both healthy subjects and ICH patients. Finally, they were tested on cardiac QSM of healthy subjects.

Implementation details

For P_{emp} (Eq. 5) and $P_{\text{emp}+R_2^*}$ (Eq. 6), the weight P_S was chosen as 30 for brain/head QSM (30) and 20 for cardiac QSM (24). In estimating the approximate solution χ_{est} , PDF was performed with 5 CG iterations for sources outside M . For sources inside M , LBV was performed with a 3-voxel erosion of the ROI mask M to exclude noisy field measurements at the boundary, followed by TKD with a threshold of 0.2. At the weight generation stage, the nonlinear least squares fitting for parameters $(\sigma_0, \sigma_1, \sigma_2, r_0, s_1, s_2)$ was performed using Matlab's *fmincon* routine. The distance map $\mathcal{D}$ was calculated using the method in (43), which iteratively searched for the closest point within the boundary of M for each external voxel, and used their distances as the value in the map $\mathcal{D}$. This particular distance transform algorithm was employed for its ability to calculate Euclidean distance in the presence of anisotropic voxel size, as required in our experiment. More details can be found in (43). For brain/head QSM, $\lambda_1 = 0.001$ and $\lambda_2 = 0.1$ were used in (Eq. 4), with M_2 chosen as ventricular CSF which can be automatically generated from multi-echo magnitude images (37). Susceptibility values were then referenced to the mean susceptibility within M_2 . For cardiac QSM, $\lambda_1 = 0.001$ and $\lambda_2 = 0.2$ were used. The Gauss Newton Conjugate Gradient (GNCG) solver was implemented as in (30), except for the choice of numerical conditioning parameter ϵ for calculating the weak derivative of the L1-norm in Eq. 4: More specifically, $M_G \nabla P y$ was replaced with $\sqrt{|M_G \nabla P y|^2 + \epsilon}$ to avoid division by zero, see Appendix in (30). In (30), ϵ was chosen as 10^{-6} for all voxels. In this work, we chose $\epsilon = P^2 \times 10^{-6}$ such that the numerical conditioning weight would remain approximately 10^{-6} for weak susceptibility tissue ($P \approx 1$) but increase for strong susceptibility sources ($P > 1$). The goal of this

increased conditioning weight is to accelerate GNCG convergence (44). The reader is directed to Supporting Information: numerical conditioning parameter and Supporting Information Figure S1 for more details about the effects of this numerical conditioning parameter. The GNCG solver is stopped when the relative update of the norm of the susceptibility map $\|\Delta\chi\|_2/\|\chi\|_2$ is lower than 0.01.

Simulation

A numerical head phantom of size 180×220×128 was constructed from a Zubal phantom (45) with known susceptibilities simulating different brain tissues (46): white matter (WM) -0.046 ppm, gray matter (GM) 0.053 ppm, thalamus (TH) 0.073 ppm, caudate nucleus (CN) 0.093 ppm, putamen (PU) 0.093 ppm, globus pallidus (GP) 0.193 ppm, superior sagittal sinus (SSS) 0.27 ppm and cerebrospinal fluid (CSF) 0 ppm. Air (9 ppm), muscle (0 ppm) and skull (-2 ppm) were distributed outside the brain (Figure 2a). This phantom was then used to simulate two different scenarios: (A) non-ICH and (B) ICH. ICH was represented by a spherical susceptibility source of 2ppm located inside the brain mask (Figure 3a). In both cases, the total field was computed from the true susceptibility map using the forward relation: $f = d * \chi$. Gaussian white noise (SNR=100) was added to this field. R2* was also simulated for each tissue type: WM 20, GM 20, TH 20, CN 30, PU 30, GP 45, SSS 45, CSF 4 and ICH 100 (unit s⁻¹). For each iteration i , the root mean square error (RMSE) $\sqrt{\frac{1}{N} \sum_i (M\chi_i - M\chi_{T,i})^2}$ between the estimated brain susceptibility $M\chi_i$ and the ground truth $M\chi_T$, and the average susceptibilities of CN and GP were calculated as metrics of reconstruction accuracy.

In vivo experiment: neural

5 healthy subjects and 5 ICH patients were scanned at 3T (GE, Waukesha, WI) using a multi-echo GRE sequence with monopolar readout. The imaging parameters were: FA = 15, FOV = 25.6 cm, TE₁ = 4.5 – 5.0 ms, TR = 39 – 49 ms, #TE = 6 – 8, TE = 4.6 – 5 ms, acquisition matrix = 512×512×64–144, voxel size = 0.5 × 0.5 × 1 – 0.47 × 0.47 × 2 mm³, BW = ± 62.5 kHz and a total scan time of 4 – 7 min. For healthy subjects, the scan was repeated with the same scanning parameters 5 times for each subject, where the subject moved her/his head between scans to achieve 5 different B0 orientations with respect to the head: neutral, positive and negative yaws and pitches, and multiple volumetric data were registered and used for COSMOS (47) reconstruction of a ground truth brain QSM, with the brain mask generated by BET (48). For ICH patients, only the neutral head position was acquired.

At one orientation, the total field was estimated from multi-echo GRE images (49) followed by graph-cut based phase unwrapping SPURS (50). The ROI mask M for the entire head was determined by thresholding the magnitude image I : $M = I > 0.15 \times I_{\max}$, where $I_{\max}$ is the largest voxel value in I . The R2* map was estimated using ARLO (51). TFI with different preconditioner choices P_{emp} (Eq. 5), $P_{\text{emp}+R2^*}$ (Eq. 6) and P_{auto} (Eq. 9) was used to reconstruct the whole head QSM. Upon QSM reconstruction, the susceptibility of CN and GP were measured within manually drawn ROIs.

For healthy subjects, the same ROI measurement was also applied to COSMOS, and linear regression on susceptibility measurements between TFI and COSMOS were performed over all voxels inside the brain for each preconditioner choice. For ICH patients, the mean susceptibility within a 5mm-wide layer surrounding the ICH site (segmented by an experienced radiologist) was computed for each QSM, to quantify the hypo-intense artifact around the ICH (30).

In vivo experiment: Cardiac

Chest MRIs of 3 healthy subjects were performed on 1.5T (GE, Waukesha, WI) using a breath-hold electrocardiographic-triggered 2D multi-echo GRE in the short-axis view. The imaging parameters were: $TE_1 = 3.6$ ms, $TR = 23$ ms, $\#TE = 8$, $TE = 2.2$ ms, in-plane voxel size = 1.25×1.25 mm³, slice thickness = 5 mm, $\#slices = 20$, slice gap = 0. Flow compensation was applied in the readout and slice directions. Acceleration factor $R = 1.5$, with one slice scanned at each breath-hold of approximately 15 s each. The average scan time was ~12 min. The total field was estimated from multi-echo GRE images using SPURS (50) for graph-cut based unwrapping and IDEAL for water/fat separation. The $R2^*$ map was calculated using ARLO (51). TFI with different preconditioner choices P_{emp} (Eq. 5), P_{emp+R2^*} (Eq. 6) and P_{auto} (Eq. 9) were used to reconstruct QSM. The susceptibility difference between right ventricle (RV) and left ventricle (LV) was measured on the QSM for each method using manually drawn ROIs. Then the blood oxygenation difference ΔSaO_2 between arterial blood (LV) and venous blood (RV) was calculated from the susceptibility difference $\Delta\chi$ (unit: ppm) using the relation: $\Delta SaO_2 = \frac{\Delta\chi}{9.49 \times 0.151}$ (24).

RESULTS

Simulation

Results from the non-ICH scenario are shown in Figure 2. All three preconditioner choices reached $RMSE < 0.0051$ ppm at 900 CG iterations, while P_{auto} achieved the lowest RMSE (Figure 2b). The CG iteration number needed by each preconditioner in order to converge to the $\pm 5\%$ range around the true value of each ROI were 170 (P_{emp}), 550 (P_{emp+R2^*}) and 180 (P_{auto}) for the CN (Figure 2c); 260 (P_{emp}), 70 (P_{emp+R2^*}) and 170 (P_{auto}) for the GP (Figure 2d).

Results from the ICH scenario are shown in Figure 3. For ICH TFI, both P_{emp+R2^*} and P_{auto} reached $RMSE < 0.005$ ppm at 1000 CG iterations with lower RMSE for P_{auto} , while the RMSE using P_{emp} failed to go below 0.010 ppm (Figure 3b). The CG iteration number needed by each preconditioner in order to converge to the $\pm 5\%$ range around the true value of each ROI were 90 (P_{emp}), 400 (P_{emp+R2^*}) and 90 (P_{auto}) for the CN (Figure 3c); 260 (P_{emp+R2^*}), 100 (P_{emp+R2^*}) and 110 (P_{auto}) for the GP (Figure 3d). Figure 4 shows the QSMs reconstructed by each method at the 1000th CG iteration and their corresponding difference maps with respect to the truth. The larger RMSE can be appreciated from the hypo-intense artifact around the ICH in the P_{emp} result.

In vivo experiment: healthy head

ROI measurements for the CN and GP across all five healthy subjects are summarized in Figure 5a. The average differences relative to COSMOS were -5% (P_{emp}), -45% ($P_{\text{emp}+R2^*}$) and -6% (P_{auto}) for the CN and -9% (P_{emp}), -3% ($P_{\text{emp}+R2^*}$) and -4% (P_{auto}) for the GP. ROI measurement per subject can be found in Supporting Information Figure S2. The linear regression of brain tissue susceptibilities between TFI and COSMOS showed slopes of 0.77 for P_{emp} , 0.67 for $P_{\text{emp}+R2^*}$ and 0.76 for P_{auto} across the five subjects. Detailed slope estimate per subject can be found in Supporting Information Table S1.

An example of whole head TFI reconstruction of one healthy subject is shown in Figure 6. It was noted that with the $R2^*$ threshold (30 s^{-1}) used in $P_{\text{emp}+R2^*}$, regions with higher $R2^*$ such as the GP were assigned the same weight ($P_S = 30$) as the background. In contrast, P_{auto} adaptively assigned weights to different regions according to their $R2^*$ values (Eq. 7). Figure 6 also showed the QSM reconstructed by COSMOS, TFI with P_{emp} , $P_{\text{emp}+R2^*}$ and P_{auto} . The whole head QSM obtained using P_{auto} was visually similar to P_{emp} as well as COSMOS. Meanwhile, the gray/white matter contrast was less distinct in the $P_{\text{emp}+R2^*}$ outcome, especially at the boundary of the CN. This was confirmed by the CN susceptibility measurement for this subject: 0.058 ppm for COSMOS, 0.054 ppm for P_{emp} , 0.023 ppm for $P_{\text{emp}+R2^*}$ and 0.050 ppm for P_{auto} .

In vivo experiment: ICH brain

$P_{\text{emp}+R2^*}$ significantly under-estimated the CN susceptibility compared to P_{emp} and P_{auto} , as shown by the ROI measurements (Figure 5b): across 5 patients, the average CN measurement was 0.068 ppm for P_{emp} , 0.040 for $P_{\text{emp}+R2^*}$ and 0.067 ppm for P_{auto} . The average GP measurements were 0.168 ppm for P_{emp} , 0.219 for $P_{\text{emp}+R2^*}$ and 0.211 ppm for P_{auto} . The ROI measurements per subject can be found in Supporting Information Figure S2. A QSM for each of the 5 ICH patients is shown in Figure 7. A hypo-intense artifact around the ICH site present for P_{emp} was reduced for $P_{\text{emp}+R2^*}$ and P_{auto} . The mean susceptibility within a 5mm-wide layer surrounding the ICH site is shown in the lower right hand corner of each QSM, indicating an average increase of 0.061 ppm for $P_{\text{emp}+R2^*}$ and 0.060 ppm for P_{auto} , compared to P_{emp} .

In vivo experiment: Cardiac

Figure 8 shows cardiac QSM in the 3 healthy subjects reconstructed by TFI using P_{emp} , $P_{\text{emp}+R2^*}$ and P_{auto} . Under-estimation was observed in the $P_{\text{emp}+R2^*}$ result for RV-LV susceptibility measurements compared to P_{emp} and P_{auto} , as well as in the converted blood oxygenation difference SaO_2 : 14.7%~23.4% for P_{emp} , 5.2%~11.8% for $P_{\text{emp}+R2^*}$ and 18.5%~26.1% for P_{auto} . A reference value for the blood oxygenation difference in healthy subjects is 18.8% (52).

Discussion

A novel algorithm to automatically construct a general adaptive preconditioner for QSM is described using the total field and $R2^*$ derived from the input gradient echo data. This automated adaptive preconditioner overcomes the limitations of binary values and manual selection in the previous implementation of preconditioned QSM (30). Our data have shown that the automated adaptive preconditioner achieves the lowest error metrics in numerical simulation compared to the previous $R2^*$ based preconditioners. The automated adaptive preconditioner suppresses hemorrhage-related artifacts and preserves the surrounding brain tissue contrast at the same time.

An important benefit of preconditioned QSM is the elimination of errors in traditional QSM reconstruction which involves two separate steps: background field removal and local field inversion. Background field removal is intended to address the drastic contrast between background susceptibility sources such as air and bone, and local sources including parenchymal tissues. The fitting processes are intrinsically separated and hence suffer from error propagation from unresolved background field into inverted local susceptibility (30). To address this error propagation, Laplacian based methods are proposed (53–57) that facilitate implicit background field removal. They avoid the sequential fitting of the background and local field by applying the Laplacian operation to the forward signal model (1,58), which intrinsically removes the harmonic background field component. Nevertheless, the Laplacian implementation requires erosion of the region of interest (ROI) due to unreliable phase measurements beyond the ROI boundaries, therefore preventing a complete depiction of the brain parenchyma (59).

The development of preconditioning for accelerating the conjugate gradient (CG) solver has been discussed in-depth throughout the numerical optimization literature (60,61). While traditional methods involve spectrum analysis of eigenvalues of the system matrix, direct application of such an approach to the TFI reconstruction problem is challenging due to the matrix size and the intrinsic convolution operation. Although recent work has shown that a preconditioner can be constructed in k-space to approximate the inverse of the dipole kernel and gradient operator (62), its implementation for TFI is not straightforward due to the presence of the SNR weighting w and morphology constraint M_G in Eq. 4. Meanwhile, research has also focused on developing a preconditioner by leveraging prior information of the unknown solution, leading to a branch called prior-enhanced preconditioning (63–65). The behavior of the preconditioned CG is related to a generalized Tikhonov regularization:

$$\underset{\chi}{\operatorname{argmin}} \|A\chi - b\|_2^2 + \lambda_{\text{Tik}} \|\Gamma\chi\|_2^2$$

The principle idea is that, one can construct a whitening operator Γ simulating the inverse covariance matrix Σ^{-1} by $\Gamma^H\Gamma \approx \Sigma^{-1}$, if the prior distribution of χ is known as a Gaussian distribution $\chi \sim \mathcal{N}(0, \Sigma)$. It has been shown (64,65) that, if a preconditioner P is chosen such that $P^{-1} \approx \Gamma$, improved convergence is obtained when solving the following problem:

$$\chi = Py, \quad \underset{y}{\operatorname{argmin}} \|APy - b\|_2^2$$

This provides a guideline for choosing a preconditioner P : the transformed variable $P^{-1}\chi$ should have unit variance: $P^{-1}\chi \sim \mathcal{N}(0, I)$. In other words, P should be proportional to the presumed susceptibility magnitude of each voxel. By this guideline, a binary preconditioner was employed in the previous TFI work (30), in which an empirical weight, 30, was assigned to strong susceptibility sources such as air, bone and hemorrhage, whereas weight 1 was assigned to soft tissues with weak susceptibility sources. The current work gives the preconditioner more flexibility in depicting the spatial distribution and dynamic contrast of the susceptibility map. It efficiently generates an approximated solution χ_{est} from the field input using PDF and LBV+TKD, and the absolute susceptibility value in χ_{est} was used in constructing the preconditioning weights. It is noted that, instead of directly using $|\chi_{\text{est}}|$ at each voxel, we group voxels by their spatial (distance towards object's boundary) or relaxational property (R2*), and calculate the median value of the observed absolute susceptibility value within each group. This approach aims to mitigate the influence of the noise and artifact in a single voxel, while median is chosen due to its robustness against outliers.

R2* information is essential in our preconditioning technique, since it depicts the location of strong susceptibility tissues within the subject, such as ICH. As seen in the simulation (Figure 4) and in vivo experiment (Figure 7), incorporation of R2* in the preconditioner ($P_{\text{emp}+R2^*}$ and P_{auto}) markedly suppressed the hypo-intense artifacts surrounding the ICH sites. Otherwise the QSM may suffer from qualitative and quantitative degradation, especially for structures close to the ICH, as observed in the under-estimation of the GP in Figure 3d. Previous work (30) employed a simple binary threshold framework to differentiate weak/strong sources by their R2* and assigned the same weight to high-R2* regions as it did to the background. The proposed method incorporates R2* contrast into the construction of preconditioner in a more adaptive manner. After we obtain a rough estimate of tissue susceptibilities, a sigmoid function σ (Eq. 7) is employed to simulate the monotonic relation between R2* and observed absolute susceptibility value χ^{med} . This monotone relation incorporates the prior knowledge that a higher R2* value typically implies larger absolute susceptibility value, as in the case of hemorrhage (strongly positive value) or calcification (strongly negative value). An alternative perspective is to treat susceptibility χ_i at each voxel as a random variable dependent on the value of R2* value $\mathcal{R}$, with the conditional probability distribution $\mathcal{N}(0, \sigma^2(\mathcal{R}))$. Using $\sigma(\mathcal{R})$ as the preconditioning weight, $P^{-1}\chi$ presumably has unit variance. It is noted that if $\sigma_1 = 1$, $\sigma_2 = 30$, $s_1 = 30$, $s_2 \ll 1$, the sigmoid function (Eq. 7) reduces to the hard threshold used in $P_{\text{emp}+R2^*}$. Therefore, the proposed preconditioner can be thought of as a generalized version of its empirical counterpart. Figure 9 shows how the fitted sigmoid function accounts for different dynamic contrasts in non-ICH and ICH subjects: compared to a non-ICH brain, the ICH data

produces a sigmoid curve with much higher σ_2 , which corresponds to an increased population of ICH voxels at the high- $R2^*$ -high-susceptibility area. This built-in scalability preserves the capability to suppress ICH-related artifacts (Figure 4 and Figure 7) and addresses the under-estimation issue in the previous empirical choice $P_{\text{emp}+R2^*}$ for structures such as the CN.

The proposed automatic preconditioner construction method is readily applicable to the QSM problem outside the head. The previous empirical choice (30) requires a new search for preconditioning weights for each anatomy and application. This is avoided in the proposed method, which achieves lower reconstruction RMSE (Figure 2b and 3b) and reliable ROI measurements (Figure 5a). When applied to cardiac QSM, the proposed P_{auto} produces a reasonable estimation for the LV-RV oxygenation level difference (18.5%~26.1%), which is more comparable to the reported level of 18.8% (66) than to the measurement by the empirical preconditioner $P_{\text{emp}+R2^*}$ (5.2%~11.8%).

The current work is still limited in the following aspects, and possible solutions are proposed accordingly for further study: 1) Construction of the preconditioner in Eq. 9 requires $R2^*$ information, which is unavailable in single-echo acquisitions. One workaround is to replace the sigmoid function in Eq. 7 with a simple uniform value which can be the median or mean over all absolute susceptibilities inside M , although an inferior ability to suppress ICH-related artifacts are expected. An alternative solution to the absence of $R2^*$ might be utilizing other image contrasts such as T1w or T2w as the variant in Eq. 7 in place of $R2^*$. 2) The preconditioner construction relies on an approximate map χ_{est} for the expected susceptibility map. Currently we use PDF and LBV+TKD to estimate sources out- and inside M , respectively. This rough estimate of susceptibility still contains substantial noise or artifacts (e.g. due to low SNR in ICH). One might improve the preconditioner by providing a better estimation χ_{est} that is more robust against noise and artifacts. For example, the final reconstructed QSM by TFI can be used as χ_{est} and utilized to initiate a new round of TFI reconstruction with the updated preconditioner, at the cost of doubled overall reconstruction time. 3) The proposed P_{auto} sometimes required more iterations than P_{emp} or $P_{\text{emp}+R2^*}$ for recovering the CN and GP (Figs. 2c and 2d). This suggests that P_{auto} might not improve convergence in all parts of the brain, even though its overall RMSE decreases the fastest (Fig 2b). This can potentially be addressed using a more accurate χ_{est} as mentioned earlier. 4)

The whole head mask used in this work was determined using a fixed threshold in each case. Automated skull masking has been researched in neuroimaging and could be incorporated here. 6) In the cardiac experiment, we were using a breath-hold 2D multi-slice acquisition which might be susceptible to a potential phase inconsistency between slices due to motion. This can be improved using a fully 3D multi-echo cardiac sequence, but it has to be time efficient and preferably free of breath holding. 7) The performance of the proposed preconditioned method will be assessed on more image content, such as in carotid, musculoskeletal and animal QSM.

CONCLUSION

An automated adaptive preconditioner is described for QSM reconstruction, which allows total field inversion without background field removal. The automated adaptive preconditioner adapts to the actual susceptibility content using the total field and $R2^*$ derived from the input gradient echo data. The automated preconditioner improves convergence speed and accuracy in reconstruction iterations and produces reliable susceptibility measurements in brain and cardiac QSMs, particularly in suppressing hemorrhage-associated artifacts while preserving surrounding normal tissue contrast.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Flow chart for generating the preconditioner P_{auto} from a total field f and a soft tissue ROI mask M . An approximate susceptibility map χ_{est} is estimated using PDF and LBV+TKD for sources out- and inside M , respectively. Voxels outside M are grouped by their distance $\mathfrak{D}$ towards the boundary of M , and the median absolute susceptibility χ^{med} within each group is calculated and then fitted to a cubically decay function with respect to $\mathfrak{D}$. Voxels inside M are grouped by their R2* value $\mathcal{R}$ and the median absolute susceptibility χ^{med} within each group is calculated and then fitted to a sigmoid function with respect to $\mathcal{R}$. The fitted value for mean absolute susceptibility of each voxel is taken as the weight in the preconditioner P_{auto} .

Figure 2.

Simulation results for non-ICH scenario. True susceptibility map χ_T (a), root-mean-square-error (RMSE) between the reconstructed and true QSM (b), ROI measurement for CN (c) and GP (d) at different CG iteration. P_{auto} achieved the lowest RMSE among the three methods. Under-estimation of CN was consistently observed for $P_{\text{emp}+R2^*}$ compared to P_{emp} and P_{auto} .

Figure 3.

Simulation results for ICH scenario. True susceptibility map χ_T (a), root-mean-square-error (RMSE) between the reconstructed and true QSM (b), ROI measurement for CN (c) and GP (d) at different CG iteration. P_{auto} achieved the lowest RMSE among three methods. At 1000th CG, P_{emp} has a much larger RMSE than those of $P_{\text{emp}+R2^*}$ and P_{auto} . Under-estimation of CN was consistently observed for $P_{\text{emp}+R2^*}$ compared to P_{emp} and P_{auto} . For GP measurement, P_{emp} showed a bias of -3% at 1000th CG, while the bias of $P_{\text{emp}+R2^*}$ and P_{auto} was -0.6% and -0.7%, respectively.

Figure 4.

Simulation result for ICH scenario: true brain QSM and brain QSM reconstructed by TFI using P_{emp} , $P_{\text{emp}+R2^*}$ and P_{auto} at the 1000th CG iteration (top row). Difference with respect to the true QSM was also shown (bottom row). Strong hypo-intense artifact around the ICH was present in P_{emp} result, leading to larger RMSE with respect to true brain susceptibilities shown in Figure 3b. This artifact over-shadowed part of the nearby GP.

Figure 5.

ROI measurements averaged over 5 healthy subjects (left) and 5 ICH patients (right), respectively, for CN and GP. Underestimation was found in $P_{\text{emp}+R2^*}$ in measuring CN, compared to P_{emp} and P_{auto} . For GP, P_{emp} gave significant under-estimation for GP in ICH patients compared to P_{auto} and $P_{\text{emp}+R2^*}$.

Figure 6.

Example of preconditioning one healthy subject using COSMOS as reference. Top row: preconditioner maps of P_{emp} , $P_{\text{emp} + R2^*}$ and P_{auto} . Middle row: QSM for COSMOS, P_{emp} , $P_{\text{emp} + R2^*}$ and P_{auto} . Difference between each map with COSMOS is shown in the bottom row. P_{emp} and P_{auto} obtain similar results for the entire head and comparable results with COSMOS for the brain. The contrast between CN and surrounding whiter matter is less distinct in $P_{\text{emp} + R2^*}$ compared to other maps. This low contrast is also identified using large difference in the same region.

Figure 7.

QSM for 5 patients with ICH. Hypo-intense artifacts are observed around the ICH site in the output of P_{emp} , while they are suppressed on both $P_{\text{emp}+R2^*}$ and P_{auto} . The mean susceptibility value within a 5mm-wide layer outside the ICH is noted at the right-bottom corner of each map. The increase in this susceptibility measurement, as observed in $P_{\text{emp}+R2^*}$ and P_{auto} compared to P_{emp} , reflects the reduced hypo-intense artifact.

Figure 8.

Cardiac QSM results for 3 healthy subjects. From top to bottom: magnitude image at short-axis view, QSM reconstructed using P_{emp} , $P_{\text{emp}+R2^*}$ and P_{auto} . Oxygenation level difference between LV and RV calculated from the susceptibility difference between LV and RV is noted at the bottom right-hand corner of each map, indicating under-estimation by $P_{\text{emp}+R2^*}$ compared to P_{emp} and P_{auto} .

Figure 9.

Comparison of non-ICH subject (top row) and patients with ICH (bottom row). QSM (1st column) and $R2^*$ map (2nd column) are displayed with the corresponding $R2^*$ - $|\chi|$ scatterplot shown on the right. Notice the difference in vertical range. Pink cross denotes the median absolute susceptibility χ^{med} over all voxels contained in each $1-s^{-1}$ bin of $R2^*$. A sigmoid function (red curve) is then fitted to the relation between $R2^*$ and χ^{med} .