Published in final edited form as:

Magn Reson Med. 2015 February ; 72(2): 697–703. doi:10.1002/mrm.25155.

Iterative Projection Onto Convex Sets for Quantitative Susceptibility Mapping

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Abstract

Purpose—Quantitative Susceptibility Map (QSM) reconstruction is ill posed due to the zero values on the “magic angle cone” that make the maps prone to streaking artifacts. We propose Projection Onto Convex Sets (POCS) in the method of Steepest Descent (SD) for QSM reconstruction.

Methods—Two convex projections, an object-support projection in the image domain and a projection in k-space were used. QSM reconstruction using the proposed SD-POCS method was compared to SD and POCS alone as well as with truncated k-space division (TKD) for numerically simulated and 7 T human brain phase data.

Results—The QSM reconstruction error from noise-free simulated phase data using SD-POCS is at least two orders of magnitude lower than using SD, POCS or TKD and has reduced streaking artifacts. Using the l_1 -TV reconstructed susceptibility as a gold standard for 7 T *in vivo* imaging, SD-POCS showed better image quality comparing to SD, POCS or TKD from visual inspection.

Conclusion—POCS is an alternative method for regularization that can be used in an iterative minimization method such as SD for QSM reconstruction.

INTRODUCTION

Quantitative Susceptibility Mapping (QSM) (1–4) is a new MRI technique that maps the magnetic susceptibility using the phase of a gradient echo image. It provides quantitative susceptibility contrast of local tissues and is useful for quantifying the iron concentration in the human brain (5), identifying brain dysmyelination (6), assessing *in vivo* brain iron metabolism (7), and mapping the anisotropy of the axon fibers (8,9). It is also a potential endogenous biomarker for diagnosis of brain degenerative disorders such as Alzheimer's disease, Huntington's chorea, and Parkinson's disease (10–12).

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QSM reconstruction is an inverse problem, which can be solved using the convolution theorem or iterative methods such as Steepest Descent (SD) or Conjugate Gradient (CG). However, the QSM inverse problem is underdetermined and ill posed due to zero values on the “magic angle” double conic surface aligned at 54.7° to the main magnetic field. These singularities produce streaking artifacts in the images. The simplest approach to remove the singularities is the Truncated K-space Division (TKD) method, which applies a threshold to the k-space dipole kernel (1). TKD is computationally fast, but produces inaccurate susceptibility images. Total Variation (TV) regularization with l_1 -normalization is another method proposed to solve the QSM inverse problem (5,13). However, regularization is computationally intense and time consuming, especially for high-resolution 3D data and if nonlinear regularization is used. The zeros can also be circumvented by taking multiple measurements at different orientations with respect to the main magnetic field, as proposed by Calculation Of Susceptibility through Multiple Orientation Sampling (COSMOS) (14,15). The drawback of this method is that it requires multiple measurements, and separate studies (8,9) have proposed that the susceptibility tensor is anisotropic while COSMOS assumes that the susceptibility is isotropic.

Projection Onto Convex Sets (POCS) is an alternative to regularization that can be used to solve ill-posed problems. The theoretical framework of POCS is presented in (16) and has been widely applied to restoring images from partial data (17-19). In MRI applications POCS has been used for phase-constrained partial Fourier imaging (20), ghost artifact correction in EPI (21), motion artifact correction in angiography (22) and parallel image reconstruction (23,24). However, the drawback of POCS is that it converges slowly and a convergence may not be guaranteed if the intersection of convex sets is empty (16,23).

In this paper, we propose the use of POCS projections in the method of Steepest Descent (SD) for increased convergence speed and more accurate QSM reconstruction. For proof of concept, we implemented two simple POCS projections, an objective support projection derived from the magnitude image and a k-space projection derived from the structure of the dipole kernel. We show with numerical simulations that the error of the QSM reconstruction from noise-free phase data using SD-POCS is approximately two orders of magnitude lower than SD and one order of magnitude lower than POCS for the same number of iterations in addition to the mitigated streaking artifacts in the reconstructed susceptibility images. We also show with simulations that the QSM reconstruction using SD-POCS is more accurate and has less streaking artifacts than direct deconvolution methods such as TKD. Finally we show that QSM reconstruction of 7T *in vivo* brain phase data using SDPOCS is more accurate than TKD and has comparable quality to results from l_1 -TV.

THEORY

Qsm Reconstruction

The magnetic susceptibility χ is the deconvolution of the relative offset of the magnetic field, ΔB_z , with a unit magnetic dipole $D_r = (3\cos^2\theta - 1) / (4\pi |r|^3)$, where θ is the angle between the B_0 field and the position vector r . The field offset $\Delta B_z = -\phi / (\gamma T_2 T_0)$ is measured using a Gradient echo sequence, where ϕ is the signal phase, γ is the gyromagnetic

ratio. B_0 is the magnetic field strength, T_E is the echo time. QSM reconstruction requires solving a linear equation:

$$D\chi = \varphi \quad [1]$$

where D is the dipole kernel D_r in a matrix form, and φ is the acquired phase. χ can be solved for following the convolution theorem by taking an element-by-element division of the k-space phase φ_k by the k-space convolution kernel $D_k = 1 / (3 - k_z^2 / |k|^2)$. However, this results in singularities in the k-space susceptibility χ_k on the magic angle conic surface. These singularities produce streaking artifacts in the reconstructed QSM images.

The TKD method removes the singularities by truncating the dipole kernel with a threshold. The advantage of TKD is its fast computing speed. Its drawbacks are that the resulting susceptibility maps still have some streaking artifacts and susceptibility values are often inaccurate. An iterative optimization method such as CG or SD solves Eq. [1] by searching for a minimum value of an objective function

$$\arg \min_{\chi} \{ \|D^T D\chi - D^T \varphi\|^2 \} \quad [2]$$

where the superscript T represents the matrix transpose. Although this optimization does not involve division by zero, the linear equation is still ill posed due to the zeros in the dipole kernel.

Regularization is a standard method for solving ill posed problems. *A priori* information from the magnitude image or an assumption on the solution can be incorporated as an additional constraint into the objective function to find an optimal solution. Regularization searches for an optimal solution that satisfies Eq. [1] and the regularization term. For data acquired with a single orientation, L_1 -norm TV regularization reconstructs QSM maps with excellent quality.

Qsm Reconstruction Using Pocs

POCS is an alternative method to regularization. Similar to regularization, POCS selects a solution that satisfies both the linear equations and a constraint. In a regularization method such as TV, the assumption is that the solution should have a minimal value of variance from voxel to voxel in addition to satisfying Eq. [1]. The *a priori* information used in POCS is determinant constraints applied through projections. An example of a determinant constraint is using the magnitude image to set the susceptibility to zero for voxels outside the brain. Note that this is different than simple masking which only applies to the final solution. POCS uses this projection to update the estimated solution in iterations.

An advantage of POCS is that multiple constraints can be easily applied at the same time. In this paper, for a proof of concept we use two simple projections P_1 and P_2 . The first projection P_1 defines an object support constraint in the spatial domain. It is extracted from the magnitude images and sets χ to zero outside of a region M (the brain volume). It can be written as:

$$P_1\chi(\mathbf{r}) = \begin{cases} \chi(\mathbf{r}) & \mathbf{r} \in M \\ 0 & \text{otherwise} \end{cases} \quad [3]$$

The second projection P_2 defines data availability in the frequency domain such that data in the vicinity of the magic angle cone are not available. A threshold λ applied to D_k determines which data points can be used in the χ reconstruction. This projection can be written as

$$P_2\chi(k) = \begin{cases} \chi(k) & D_k \leq \lambda \\ 0 & D_k > \lambda \end{cases} \quad [4]$$

These two constraints are applied using the Gerchberg-Papoulis method (18), which is chosen for its simplicity. Following the GP algorithm the above two projections can be alternately applied in the spatial and frequency domain as:

$$\chi_{n+1} = P_1\mathcal{F}^{-1}\{\mathcal{F}(\chi_0) + P_2\mathcal{F}(\chi_n)\}, \quad [5]$$

where $\mathcal{F}$ and $\mathcal{F}^{-1}$ denote the Fourier transform and inverse Fourier transform, respectively. The initial value of susceptibility χ_0 can be estimated using the TKD method for example.

Qsm Reconstruction Using Sd-Pocs

Although POCS alone can be used for QSM reconstruction following Eq. [5], the drawback is that the convergence can be extremely slow. It could take as many as hundreds of thousands iterations to converge. However, the POCS approach shown in Eq. [5] can also be applied along with an iterative algorithm such as the method of SD. This approach of using a combination of the iterative TV with POCS has been proposed for low-intensity x-ray CT reconstruction (31). Although the more common CG iterative approach guarantees a faster convergence than SD, applying projections in iterations modifies the CG search direction, and as a result the modified search directions are not conjugate to each other anymore. The detailed algorithm of the implementation of SD-POCS is listed below where at iteration number n the operations are run until the desired error or number of iterations is reached:

$$\begin{aligned} \mathbf{r}_n &= \mathbf{b} - \mathcal{F}^{-1}\{D_k^H * D_k * \mathcal{F}(\chi_n)\} \\ \mathbf{r}_n &= \mathcal{F}^{-1}\{D_k^H * D_k * \mathcal{F}(\mathbf{r}_n)\} \\ \alpha &= (\mathbf{r}_n^T \cdot \mathbf{r}_n) / (\mathbf{u}_n^T \cdot \mathbf{r}_n) \\ \chi_{n+1} &= \mathcal{F}^{-1}\{\mathcal{F}(\chi_0) + P_2\mathcal{F}(\chi_n + \alpha\mathbf{r}_n)\} \end{aligned}$$

In the above equations, χ_0 is obtained using the TKD method and $\mathbf{b} = \mathcal{F}^{-1}\{L_k^H * \mathcal{F}(\phi)\}$. Also note that the computationally intensive matrix-vector DD_ϕ^T and matrix-matrix-vector multiplications $D^T D_\chi$ in Eq. [2] were replaced by the equivalent but efficient element-by-element multiplications $\mathcal{F}^{-1}\{D^H * \mathcal{F}(\phi)\}$ and $\mathcal{F}^{-1}\{D_k^H * D_k * \mathcal{F}(\chi)\}$ in k-space following the

convolution theorem, where H^* denotes complex conjugate and $*$ denotes element-by-element multiplications.

METHODS

Simulations

Numerical simulations were performed using a 3D Shepp-Logan susceptibility phantom (matrix size = $256 \times 256 \times 128$, FOV = $256 \times 256 \times 128$ mm). The phantom orientation was placed in the sagittal (y-z) plane for better display of the streaking artifacts in the reconstructed susceptibility maps. Figure 1 (a) shows a sagittal susceptibility map of the simulated phantom. The simulated image phase was calculated from the convolution of the susceptibility phantom with the magnetic dipole kernel. This phase is defined as the “true” phase of the phantom. The phase of the same slice in (a) is shown in (b). QSM reconstruction using the simulated phase was then performed with TKD, POCS, and SD-POCS. Both POCS and SD-POCS used 100 iterations or an optimization error of $1e-3$, whichever was reached first, and $\lambda = 0.2$ unless otherwise stated. All simulations and reconstructions were run on an Apple (Cupertino, CA) iMac (2.66 GHz Intel Core i5 quad-core CPU and 16 GB RAM) using Mathworks (Natick, MA) Matlab (2012b).

Three different comparisons were performed on the simulated phase data. First, to show the effect the projections had on the convergence of SD-POCS, the use of each individual projection (P_1 and P_2) as well as both projections (P_1+P_2) was investigated. The POCS reconstruction used both projections (P_1+P_2). Second, because the projection P_2 depends on the selection of the threshold λ , results reconstructed using SD-POCS (P_1+P_2) with $\lambda = 5E-3, 1E-2, 2E-2, 5E-2, 8E-2, 1E-1$, and $2E-1$ were also compared. Finally, to study the reconstruction with different noise levels, Gaussian noise with various standard deviations ($1E-5, 5E-5, 1E-4, 5E-4, 1E-3$) was added to the phase images as well. The square root of the sum of the square difference between the reconstructed and the true χ, ϵ_{χ} , is used to quantify the reconstruction error in simulations.

In Vivo Imaging

In vivo susceptibility maps of normal human brains, acquired on a 7T Magnetom Siemens (Erlangen, Germany) scanner with an eight-channel head coil, were also reconstructed using TKD, POCS, and SD-POCS (P_1+P_2). Susceptibility maps were also reconstructed using l_1 -TV regularization as a “gold standard” reference for a qualitative comparison. POCS, SD-POCS, and l_1 -TV all use 100 iterations or an optimization error of $1e-3$, whichever was reached first, and $\lambda = 0.2$. Three subjects were scanned with informed consent obtained according to a University of Pittsburgh IRB approved protocol. The imaging sequence was a gradient- and RF-spoiled multi-echo 3D gradient echo sequence (FA = 15° , TR = 24 ms, TE = 7.14, 11.12, 15.30, 19.38 ms, voxel size = $0.5 \times 0.5 \times 1.5$ mm, matrix size = $448 \times 336 \times 64$).

The human phase images underwent preprocessing prior to QSM reconstruction. The complex images from each coil were first reconstructed individually. The magnitude images from all coils were then combined using the sum-of-squares method and processed using FMRIB's Brain Extraction Toolbox (BET) to remove non-brain tissues (25). A binary mask was created from the magnitude images for the TKD reconstruction and the P1 POCS

projection. The phase images for all coils at each echo were then unwrapped using a 3D unwrapping algorithm (26). A phase offset for each coil was calculated using the phases from the first and second echoes as discussed in (27) and applied to the complex image of each coil to correct phase offsets. Finally the combined phase was calculated as the angle of the sum of complex images from all eight channels.

As part of the preprocessing, the background phase needs to be removed from the total phase because the phase shift produced by the susceptibility gradients at the air-tissue boundaries can be up to one order higher than the phase from the local tissue susceptibility. We used the recently proposed Projection into Dipole Fields (PDF) method (28) to remove the background phase. Two hundred iterations were used to ensure an accurate local phase map as suggested in the literature (5). The total time for removing the background phase for one subject was approximately 45 minutes. A faster toolbox is available at <http://weil.cornell.edu/mri/QSM/QSM.htm>.

RESULTS

Simulations

From left to right, Fig. 2 (a) shows the susceptibility maps in the sagittal plane reconstructed using L_1 -TV, TKD, POCS, SD, SD-POCS (P_1), SD-POCS (P_2), and SD-POCS (P_1+P_2), respectively. The differences between the reconstructed and the true susceptibility maps are shown in (b) in the same order. The effect of applying individual projections P_1 and P_2 within SD-POCS can be observed in this figure. Applying P_1 mitigates the streaking artifacts and P_2 reuses the k-space points that are thresholded out by TKD, and therefore leads to a more accurate susceptibility. The susceptibility maps from SD-POCS (P_1+P_2) appear to be the most accurate and have least streaking artifacts compared to the other four methods. The reconstruction error ε_χ as a function of iterations is shown in (c) for the reconstruction methods. SD-POCS (P_1+P_2) has the lowest error. TKD is not shown because it is not iterative.

The convergence of SD-POCS (P_1+P_2) in terms of reconstructed susceptibility error ε_χ for different λ is shown in Fig. 3 (a). The simulated input phases were noise free. A lower threshold λ allows for more points close to the “magic angle” cone surface to be used in the calculation and results in a more accurate QSM reconstruction. The reconstruction error ε_ϕ as a function of iteration number for different levels noise is shown in (b). It can be seen that with noise in the phase data, a smaller threshold leads to more noise amplification.

In Vivo Imaging

Figure 4 shows the QSM reconstruction results of one subject. The magnitude image of an axial slice is shown in (a) for reference. The phase difference between the first echo (7.14 ms) and the second echo (11.12 ms) is shown in (b) and the corresponding unwrapped phase map is shown in (c). Note the dominating background phase produced by the air-tissue interface. This background phase was removed using the PDF method and the resultant phase from the brain tissues is shown in (d). The susceptibility reconstructed using L_1 -TV is shown in (e) for a qualitative reference. The susceptibility maps reconstructed using TKD, POCS, and SD-POCS (P_1+P_2) are shown in (f), (g), and (h), respectively. From visual

inspection, the susceptibility map from SD-POCS (P_1+P_2) is more similar to the maps obtained from l_1 -TV regularization than from TKD and POCS. Figure 5 shows example susceptibility maps in the coronal plane. The coronal orientation better displays the streaking artifacts. The susceptibility maps reconstructed using l_1 -TV regularization, TKD, POCS, and SD-POCS are shown in (a), (b), (c), and (d), respectively. Other subjects and slices showed qualitatively similar results. The reconstruction times for SD-POCS and l_1 -TV were 314 and 685 seconds, respectively.

DISCUSSION AND CONCLUSIONS

In this paper, we proposed an iterative SD-POCS method for QSM reconstruction. The reconstruction error ε_χ in the reconstruction of the susceptibility from the simulated noise-free phase data was approximately two orders of magnitude lower than from using SD or POCS alone. Comparing to the direct deconvolution methods such as TKD, SD-POCS yielded more accurate susceptibility values with less streaking artifacts and less minimization error. In this work a spatial projection operator P_1 and a k-space projection operator P_2 were implemented in the GP algorithm to update the SD-POCS iterations. Shown in Fig. 2 (a), the effect of applying the spatial object-support projection P_1 is to suppress the streaking artifacts. Because the streaking artifacts exist in the entire FOV, P_1 constrains the solution to exist only in the object, changes the search direction in SD, and therefore helps to suppress the streaking artifact. Applying an object-support spatial projection is equivalent to using the Dirichlet boundary condition proposed in de Rochefort et al (30). Using P_2 leads to more accurate result but also more streaking artifacts. This is because P_2 uses values threshold out by TKD, which reduces artifacts but produces inaccurate results. The choice of λ in P_2 needs to balance the reconstruction accuracy and the degree of streaking artifacts. A smaller λ includes more data points around the magic angle conic surface in the reconstruction, but this could lead to noise amplification due to the division of phase values divided by extreme small dipole values at these regions. A higher λ can lead to susceptibility images with seemingly good quality however susceptibility values in the images may be inaccurate.

The choice of a spatial projection operator P_1 and a k-space projection operator P_2 was chose for simplicity, and numerous other projections could be useful. For example the projections in the algorithm can be replaced by relaxed projections, which can accelerate the convergence (18,23). Several projections can also be simultaneously applied for a better constraint for the ill-posed inverse problem. Other iterative techniques should also work with POCS for QSM. In this paper, the POCS was implemented in the method of SD instead of CG, which converges faster than SD. However, CG requires conjugate search directions, and a direct implementation of POCS in CG modifies the search direction therefore changes the convergence of the algorithm. A possible solution is that POCS can be applied in a second outer loop outside the CG loop, and CG can be restarted with the estimate updated by POCS in the outer loop (29).

The phase and the subsequence reconstructed QSM images seem to have different contrast than previously published result. This is likely due to the lower contrast in the phase images, and we observed that our methods produced similar QSM contrast when the test data in

Cornell QSM toolbox are used. One of the limitations of the paper is the lack rigorous mathematical proof of the convergence of the GP algorithm for the QSM reconstruction. Instead, the convergence was shown with numerical simulations. The other limitation in this study was a lack of the true susceptibility values for the in vivo data acquired with a single orientation. Instead, the susceptibility reconstructed using l_1 -TV regularization was assumed as an approximation of the true susceptibility. A future study should use COSMOS as a gold standard to validate data acquired with multiple orientations. Also Reconstruction of the 7 T *in vivo* human brain data showed that SL-POCS produced susceptibility maps with visual quality comparable to l_1 -TV regularization. The validation of the proposed QSM reconstruction could be improved by comparing the reconstructed susceptibility to the true susceptibility values of a phantom constructed using materials with known susceptibility values. No direct comparison was made between POCS and l_1 -TV regularization because the two methods are entirely different approaches for solving ill-posed inverse problems. However, an approach that combines l_1 -TV regularization and POCS has been shown to improve the imaging quality of circular cone-beam CT reconstruction (29). A similar method for MRI QSM reconstruction is of interest for future investigations.

Acknowledgments

Work supported by the National Institute of Health (R01DA019912, R01NS02DA020569). Core resources supported by the National Center for Research Resources (G12-PX003061, P20 EB011517-RR011091), National Institute of Neurological Disorders and Stroke (U54-NS056663), and the Office of National Drug Control Policy. BAP was partly funded by the DFG (German Research Foundation) grant PO 576/1-1.

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Figure 1
The simulated Shepp-Logan susceptibility phantom and the corresponding phase image in the sagittal plane parallel to the main magnetic field.

Figure 2

The top row **(a)** from left to right shows the susceptibility maps of the simulated phantom reconstructed using l_1 -TV TKD, POCS, SD, SD-POCS (P_1), SD-POCS (P_2), and SD-POCS (P_1+P_2), respectively. The second row **(b)** shows the difference between the true susceptibility (Fig. 1) and the reconstructed susceptibility in the same order. The k-space dipole threshold λ was set to 0.2 for TKD, SD-POCS (P_2), and SD-POCS (P_1+P_2). **(c)** The reconstruction errors ε_χ as a function of the number of iterations for POCS, SD, SD-POCS (P_1), SD-POCS (P_2), and SD-POCS (P_1+P_2).

Figure 3

(a) This plot shows the reconstruction error of SD-POCS, ε_x , as a function of iterations for different dipole threshold values. **(b)** This plot shows the reconstruction error as a function of iterations for different phase noises.

Figure 4

(a) An example of an axial 7 T brain magnitude image ($TE = 7.14$ ms) with non-brain tissue extracted. **(b)** The phase difference between the first echo ($TE = 7.14$ ms) and the second echo ($TE = 11.22$ ms). **(c)** The unwrapped phase difference image. **(d)** The local tissue phase with the background phase extracted from (c) using the PDF method. **(e)** The susceptibility map reconstructed using l_1 -TV with a regularization parameter ($4E-2$), **(f)** using TKD with a threshold of 0.2, **(g)** using POCS with a threshold of 0.2, and **(h)** using SD-POCS (P_1+P_2) with a threshold of 0.2 and 10 iterations. The maps in (e)-(h) were all windowed between -0.1 and 0.1 ppm.

Figure 5
Example susceptibility maps at $\pi/4$ in the coronal plane reconstructed using (a) l_1 -TV regularization, (b) POCS, (c) SD, and (d) SD-POCS (P_1+P_2). Both regularization and SD-POCS provide images with reduced streaking artifacts compared to TKD or SD.