

Inverse MRI for Tomographic Magnetic Susceptibility Reconstruction

Chen Z^{1*} and Calhoun V^{1,2}

¹The Mind Research Network and LBERI, New Mexico, USA

²University of New Mexico, ECE Dept., New Mexico, USA

***Corresponding author:** Zikuan Chen, The Mind Research Network and LBERI, Albuquerque, NM 87106, USA, Email: zchen@mrn.org

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ABSTRACT

Background: The image formation in magnetic resonance imaging (MRI) involves a cascade of transformations (such as magnetization and intravoxel dephasing) that cause a morphological mismatch between the image and source. By solving an inverse MRI problem, we may undo the MRI transformations and reproduce magnetic source from MRI data, thus implementing tomographic reconstruction of an objects interior magnetic property (such as magnetic susceptibility, χ) distribution.

Methods: A T2*-weighted MRI (T2*MRI) produces a complex-valued T2* image through the use of a gradient-recalled echo (GRE) sequence. A T2*MRI model is decomposed into two steps: 1) from a χ source map to a fieldmap via a magnetization process, and 2) from the fieldmap to a complex T2* image via an intravoxel dephasing average. Accordingly, the inverse T2*MRI model consists of two inverse computation steps. A phase image is subject to a spatial unwrapping processing if wrapped. The fieldmap assumes a phase image (unwrapped) with a scale difference. The χ source map is reconstructed from the fieldmap by solving an ill-posed dipole inversion problem through a total-variation-regularized split Bregman (TVB) iteration algorithm. Numerical simulations, phantom experiments, and *in vivo* human brain experiments are provided.

Results: 1) A T_2^* magnitude image is morphologically different from the original χ source primarily due to nonlinear magnitude calculation; 2) a T_2^* phase image conforms the χ -induced fieldmap in a small phase angle regime, but suffers from a dipole effect; and 3) the χ source map can be tomographically reconstructed from a T_2^* phase image by a computed inverse MRI model (CIMRI).

Conclusion: We can tomographically reconstruct the internal magnetic χ source distribution by solving an inverse MRI problem through a linear CIMRI model. The conventional MRI magnitude is nonlinearly related to the χ source and to the χ -induced fieldmap but does not accurately represent the original magnetic source.

Keywords: Magnetic Resonance Imaging (MRI), Computed Inverse MRI (CIMRI), magnetic susceptibility, dipole effect, dipole inversion, intravoxel dephasing, nonlinear T_2^* magnitude image, T_2^* phase unwrapping, MRI transformations.

INTRODUCTION

The concept of tomographic imaging refers to reproducing a digital image representation of object interior distribution (with respect to a physical property) and can be implemented by solving an inverse imaging problem. For example, X-ray computed tomography (CT) reproduces an internal source distribution (in terms of a physical property of X-ray attenuation coefficient) by solving an inverse Radon transformation associated with 2D fan-beam projections or 3D cone-beam projections [1,2]. In this chapter, we will address the tomographic imaging aspects of magnetic resonance imaging (MRI) in the framework of inverse imaging. In particular, we will examine T_2^* -weighted MRI (T_2^* MRI for short) and its inverse solution for magnetic susceptibility (denoted by χ) reconstruction.

MRI is widely used for non-invasively detecting the internal magnetic state of an object. For medical imaging applications, MRI provides an image representation for tissue interiors with respect to the magnetic property of tissue material. In nuclear magnetic resonance (NMR) legacy, the detection signal is described by an exponential model with a characteristic time, such as T_1 , T_2 , and T_2^* , depending on the pulse sequence used for signal detection [3,4]. Based on spatial encoding through the manipulation of gradient fields, MRI provides a discrete image representation of the spatial distribution of NMR signals, inheriting the exponential characteristic times (T_1 , T_2 , T_2^*) for image contrast mechanisms. In fact, the output of MRI is a complex-valued image in nature as a result of quadrature detection of trigonometric spin signals [3]. Conventional MRI typically only exploits the magnitude component of the complex data. More recently, there has been enthusiasm for the exploration and exploitation of the MR phases [5-8]. Recent research [9,10] has shown that the MRI magnitude is a nonlinear transformation of the internal magnetic field distribution (called a fieldmap), and it can neither faithfully represent the fieldmap nor its magnetic source (e.g. χ for T_2^* source). Furthermore, the magnitude nonlinearity is irreversible, which prevents an inverse solution. On the other hand, the MRI phase image may represent the

internal fieldmap under certain approximation conditions and after image postprocessing, thus opening an avenue to the original magnetic source reconstruction via solving an inverse imaging problem [11-13]. Unlike the MRI magnitude, the MR phase cannot be characterized by T1, T2, and T2* models. In compliance with NMR and MRI legacy, we refer to the “T2* image” as the GRE-acquired MR image and “T2* source” as the magnetic susceptibility (χ) distribution. The purpose in this chapter is to shed light on the inverse T2*MRI model and thereby to find an approach to reconstruct the T2* source.

THEORY, MODELS, ALGORITHMS

An overview of T2*MRI and its inverse is diagrammed in Figure 1. The forward T2*MRI model describes a data acquisition procedure from the input of the χ source (T2* source) to the output of the complex T2* image. The inverse T2*MRI model is proposed to reconstruct the χ source from complex T2* images [11,14]. It is noted in Figure 1 that the MRI scan and the subsequent T2* image reconstruction are designated by a pair of Fourier transform (FT) and inverse FT (IFT) procedures, which together indeed implements a tomographic reconstruction of a spatial distribution of complex-valued spin signals in the sense of Fourier-based perfect reconstruction, as denoted by an identity $IFT(FT) = 1$. An illustrative comparison on the tomographic imaging aspects of X-ray CT and MRI is provided in two supplementary figures. Although MRI is capable of tomographic imaging of an internal distribution of complex spin signals, its output (a magnitude or phase) is not a tomographic reconstruction of the χ source or the χ -induced fieldmap. (Figure 1, Supplementary Figures S1 and S2)

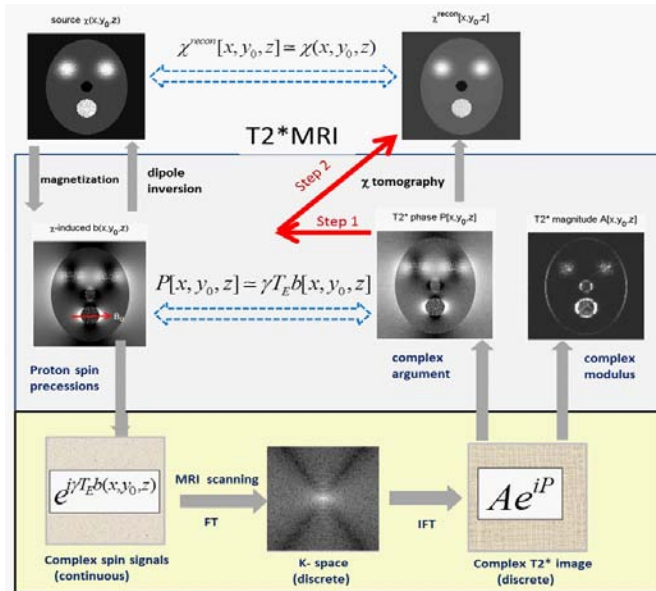
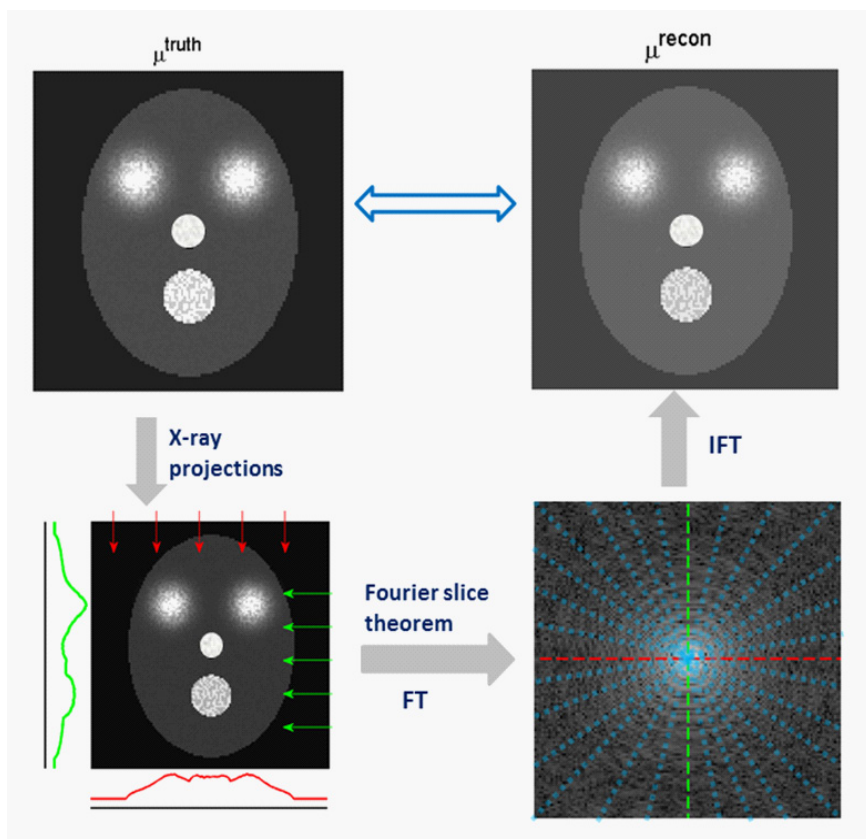


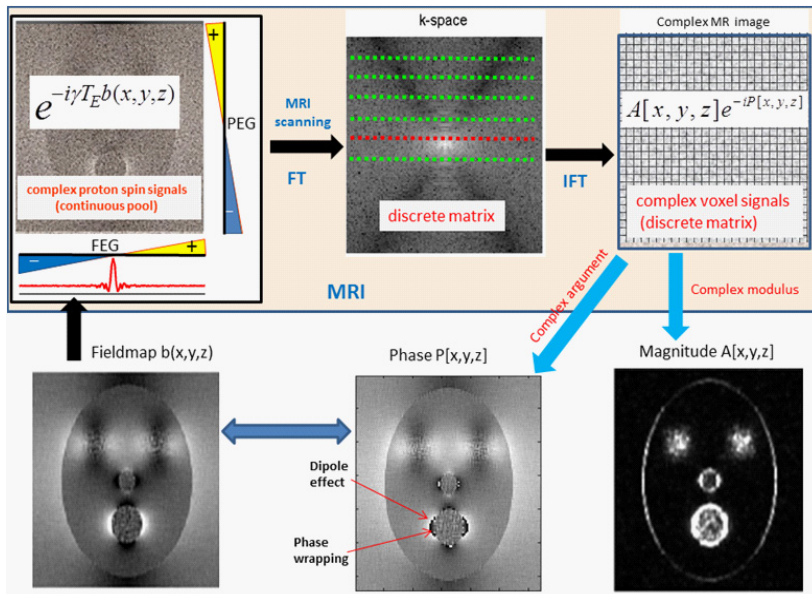
Figure 1: Diagram of T2*MRI and its inverse for magnetic susceptibility (χ) tomography.

A χ -expressed object in a main field B_0 induces an inhomogeneous fieldmap $b(x, y, z)$, which is detected by T2*MRI to produce a complex-valued T2* image in a pair of multivoxel magnitude $A[x, y, z]$ and multivoxel phase $P[x, y, z]$. A discrete χ map can be reconstructed from T2* phase image by a two-step χ tomography. The conventional MRI implements a tomographic reconstruction of the complex spin signal distribution via a pair of Fourier transform (FT) and inverse FT (IFT), but not a tomographic χ reconstruction.



Supplement Figure s1: Illustration of X-ray CT with parallel-beam projections and Fourier-based tomographic reconstruction.

The Fourier transform of a parallel-beam projection provides a slice in Fourier domain (Fourier Slice Theorem), and the X-ray attenuation coefficient map (denoted by μ) is reconstructed by a pair of Fourier transform and inverse Fourier transform (IFT). This is a conceptual illustration of CT principle with a perfect reconstruction $\text{IFT}(\text{FT})=1$, where the Fourier domain is filled with radial slices. For the sake of comparison with MRI tomography, the brain μ digital phantom is geometrically similar to the brain χ digital phantom (used in Figure 5) except for a nonnegative μ ellipsoid at the center.



Supplement Figure s2: Illustration of the tomographic imaging aspects of MRI.

The MRI scanning (through the use of a pulse sequence of spatial encoding by manipulating frequency-encoded gradient (FEG) and phase-encoded gradient (PEG)) establishes a k-space, filling the Fourier domain with rasterization lines, and the subsequent inverse Fourier transform (IFT) reconstructs a complex-valued MR image, thus implementing tomographic reconstruction of a complex distribution in the sense of $IFT(FT)=1$. However, the MR magnitude and phase calculations are nonlinear operations, causing distortions in the output images. The nonnegative MR magnitude cannot represent the internal fieldmap in any circumstance. Fortunately, the MR phase image conforms the fieldmap in small phase angle regime. In practice, a MR phase image (unwrapped) is a good tomographic reconstruction of the internal fieldmap. It is illustrated herein that a wrapped MR phase image could represent the internal fieldmap as long as the wrapping effect is appropriately removed by an unwrapping procedure.

T2*MRI and Inverse T2*MRI Models

In Figure 2, we diagrammed the forward T2*MRI model and the inverse T2*MRI model. The forward T2*MRI model in Figure 2(a) consists of two steps: from the input source χ to the fieldmap and then to the output complex T2* image (designated by two downward arrows).

The 1st step of T2*MRI is responsible for a fieldmap establishment from a χ source map via a magnetization (magnetic polarization) process in a main field B_0 , which can be expressed by a 3D convolution transformation [11, 15]

$$b(x, y, z) = B_0 \chi(x, y, z) * h_{dipole}(x, y, z)$$

$$\text{with } h_{dipole}(x, y, z) = \frac{1}{4\pi} \frac{3z^2 - |x^2 + y^2 + z^2|^{3/2}}{|x^2 + y^2 + z^2|^{5/2}}, \quad (1)$$

where $*$ denotes a spatial convolution with a dipole kernel $h_{dipole}(x,y,z)$ and $b(x,y,z)$ represents the z-components of the 3D χ -induced magnetic field distribution, which is called a fieldmap. The

3D spatial convolutional formula in Eq. (1) for χ -induced fieldmap establishment holds for linear magnetization approximation [16,17] that is valid for brain imaging (brain tissue is classified as a nonmagnetic material with $\chi_{\text{tissue}} < 10^{-6} = 1\text{ppm}$).

The 2nd step of T2*MRI produces a complex-valued image from an inhomogeneous fieldmap by an intravoxel dephasing average. Let $\exp(i\gamma T_E b(x,y,z))$ denote a proton spin precession signal at (x,y,z) over the fieldmap, where γ denotes the gyromagnetic ratio, T_E the echo time (dephasing time), then the intravoxel dephasing signal [3,10,11] is given by

$$C[x, y, z] = \frac{1}{|\Omega|} \sum_{(x', y', z') \in \Omega(x, y, z)} e^{i\gamma b(x', y', z') T_E} \quad (\text{definition})$$

$$= A[x, y, z] e^{iP[x, y, z]} \quad (\text{exponential format}) \quad , (2)$$

where $\Omega(x,y,z)$ denotes a voxel at (x,y,z) , and $|\Omega|$ the voxel size. It is noted that the intravoxel dephasing formula in Eq. (2) involves a conversion from a continuous distribution “(.)” to a discrete distribution “[.]”, which is essentially a space sampling of a continuous complex distribution with finite voxels. Although the intravoxel summation is a linear operation, the exponential complex expression on the voxel signal involves nonlinear operations (complex modulo and complex argument).

The multivoxel spatial sampling for a discrete image production is implemented by a sophisticated spatial encoding/decoding scheme through a manipulation of gradient fields [3]. The result is a discrete complex image, which is represented by a pair of magnitude and phase images, as calculated by

$$\begin{cases} A[x, y, z] = \sqrt{\left(\text{real}(C[x, y, z])\right)^2 + \left(\text{imag}(C[x, y, z])\right)^2} \\ P[x, y, z] = \arctan \frac{\text{imag}(C[x, y, z])}{\text{real}(C[x, y, z])} \end{cases} \quad , (3)$$

where the $\text{real}(C)$ and $\text{imag}(C)$ denote taking a real part and imaginary part of a complex number C respectively. The magnitude (amplitude) calculation from a complex number is a complex modulo operation, which is a nonlinear nonnegative mapping. The phase angle is calculated by $\arctan(\cdot)$, which is a nonlinear operation in general.

In order to find the relationship between the output image and the internal field, we perform Taylor expansion on the complex spin signals; that is,

$$\begin{aligned} \exp(i\gamma b T_E) &= \left[1 + i\gamma b T_E + \frac{(i\gamma b T_E)^2}{2!} + \frac{(i\gamma b T_E)^3}{3!} + \dots \right] \\ &\approx 1 + i\gamma b T_E + \frac{(i\gamma b T_E)^2}{2!} \quad (2^{\text{nd}}\text{-order approximation}) \\ &\approx 1 + i\gamma b T_E \quad (1^{\text{st}}\text{-order approximation}) \end{aligned} \quad .(4)$$

Through the use of approximations of $\arctan(x) \approx x$ and $1/(1-x) \approx 1+x$ for $|x| \ll 1$ and under 1st and 2nd-order approximations in Eq.(4), we have

$$1^{\text{st}}\text{-order approx: } \begin{cases} A[\mathbf{r}; T_E] \approx \sqrt{1 + (\gamma b[\mathbf{r}]T_E)^2} \propto (\gamma b[\mathbf{r}]T_E)^2 \\ P[\mathbf{r}; T_E] \approx \arctan(\gamma b[\mathbf{r}]T_E) \approx \gamma b[\mathbf{r}]T_E \end{cases} \quad (\text{s.t. } |\gamma b T_E| \ll 1) \quad , (5)$$

and

$$2^{\text{nd}}\text{-order approx: } \begin{cases} A[\mathbf{r}; T_E] \approx 1 + \frac{(\gamma b[\mathbf{r}]T_E)^4}{4} \propto (\gamma b[\mathbf{r}]T_E)^4 \\ P[\mathbf{r}; T_E] \approx \arctan\left(\frac{\gamma b[\mathbf{r}]T_E}{1 - (\gamma b[\mathbf{r}]T_E)^2 / 2}\right) \approx \gamma b[\mathbf{r}]T_E + \frac{(\gamma b[\mathbf{r}]T_E)^3}{2} \end{cases} \quad (\text{s.t. } |\gamma b T_E| \ll 1) . (6)$$

It is seen in Eqs. (5) and (6) that the magnitude is a nonlinear transformation in all circumstances (a quadratic mapping in the 1st-order approximation); and that the phase may assume a linear transformation in the 1st-order approximation and a cubic nonlinear transformation in the 2nd-order approximations. These approximations are subject to a small phase angle condition, $|\gamma b T_E| \ll 1$ radian, which is called a small phase angle regime [9,10]. The linear relationship between phase and fieldmap in Eqs. (5, 6) enables the internal fieldmap calculation from a T2* phase image (appropriately postprocessed). However, the magnitude nonlinearity prevents an inverse solution.

Correspondingly, the inverse T2*MRI model (diagrammed in Figure 2(b)) consists of two inverse computation steps. The 1st inverse step is to calculate a fieldmap from a complex T2* image. Under linear approximation in Eq. (5), we obtain the fieldmap from T2* phase image by

$$b^P[x, y, z] = \frac{P[x, y, z; T_E]}{\gamma T_E} \quad (\text{s.t. small phase angle regime}). \quad (7)$$

Upon calculating the phase-derived fieldmap, we proceed to calculate the χ map in the 2nd inverse step, which involves a 3D deconvolution problem, as expressed by

$$\chi^{\text{recon}}[x, y, z] = \frac{1}{B_0} b^P[x, y, z] *^{-1} h_{\text{dipole}}[x, y, z] , \quad (8)$$

where $*^{-1}$ denotes a spatial deconvolution. The 3D deconvolution with a dipole kernel (defined in Eq. (1)) is called dipole inversion. We will implement the dipole inversion by TVB [11,12] (see later).

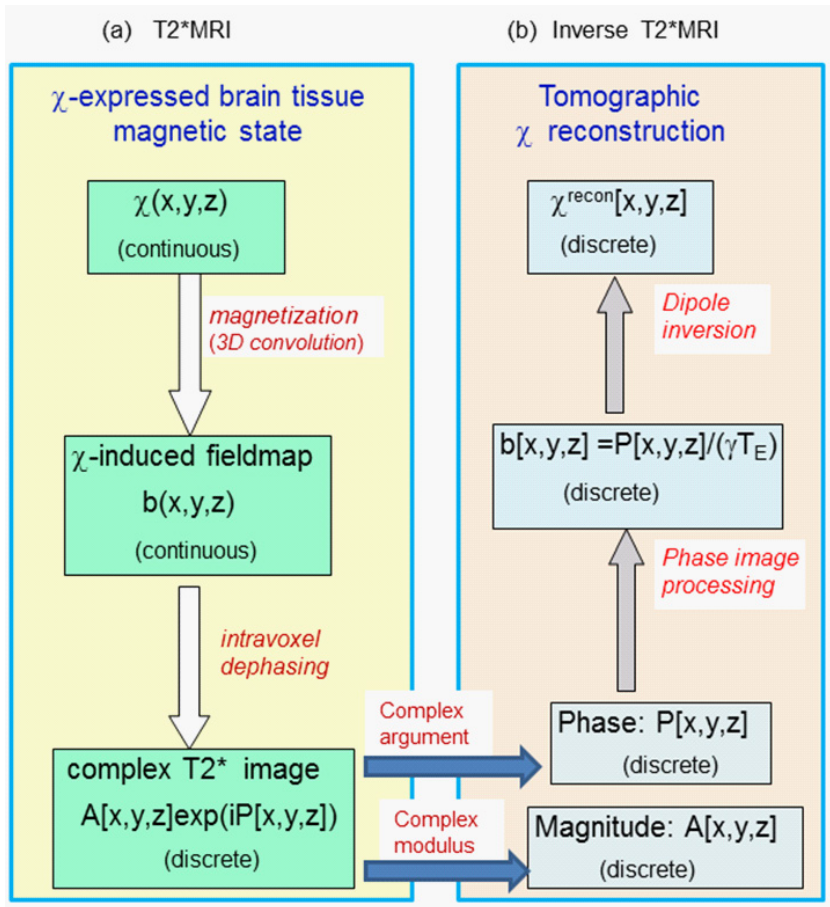


Figure 2: The forward T2*MRI and inverse T2*MRI models.

(a) The forward T2*MRI model implements a spatial mapping from a real-valued continuous χ distribution to a complex-valued discrete T2* image by two steps (marked by two downward arrows); (b) the inverse T2*MRI model implements a tomographic reconstruction of the χ source from the T2* phase image by two inverse steps (marked by two upward arrows) [14].

Dipole Effect

Under linear magnetization approximation, the fieldmap is related to its χ source by a 3D deconvolution with a dipole kernel, as expressed in Eq. (1). The dipole kernel takes on a bipolar-valued anisotropic distribution, consisting of a bowtie of double cones, as depicted in Figure 3 (a,b). The bipolar-valued distribution of the kernel defines a spatial derivative property of the 3D convolution during the χ -induced fieldmap establishment. A dipole kernel serves as a texture operator (depicted with a 2D slice in Figure 3(c)) which enhances local edges (see the standard edge operator in Figure 3(d)). It is the bipolar-valued quadrupolar pattern of the dipole kernel that causes a morphological change from χ distribution to a fieldmap [9], which is also called dipole effect [10,18,19].

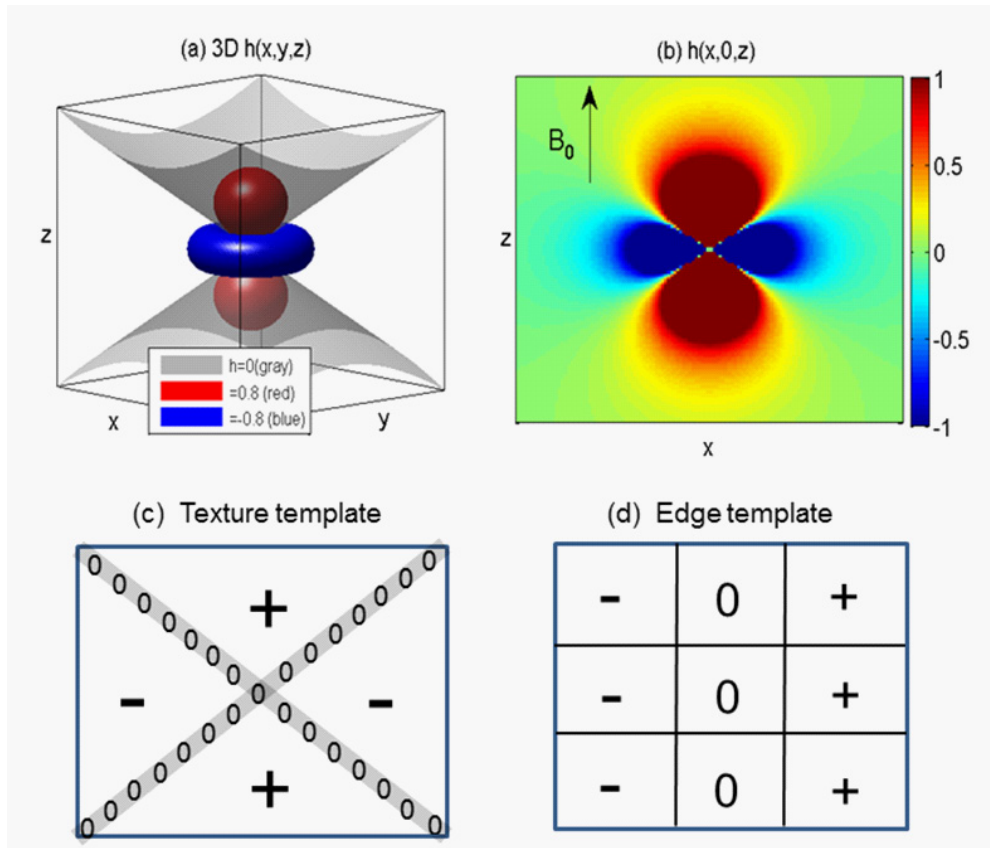


Figure 3: Illustration of the spatial derivative property of dipole-convolved magnetization.

(a) Visualization of the 3D dipole kernel ($h_{\text{dipole}}(x,y,z)$) with three isosurfaces at isovalues of $\{0, 0.8, -0.8\}$; (b) a 2D quadrupolar pattern at a longitudinal plane at $h(x,0,z)$; (c) a digital texture detector associated with (b); and (d) a standard 2D digital edge detector.) [14].

The dipole effect is inherent with a χ -induced fieldmap, and it will be propagated to the output images of MRI. Since the magnitude and phase calculations in Eq. (3) employ different nonlinear transformations on the fieldmap, the dipole effect appears in the T2* magnitude and phase images in different manifestations. Specifically, the T2* magnitude is calculated by a complex modulo operation that is a nonlinear, nonnegative transformation (polynomials of even powers) that is irreversible. The dipole effect on a magnitude image manifests as orientation dependence (with a magic angle as determined by $h_{\text{dipole}}(x,y,z) = 0$) and edge enhancement. Meanwhile, the T2* phase is calculated by an *arctan* function, which retains the signs of the fieldmap regardless of its nonlinear mapping (polynomials of odd powers). In small phase angle regime, a phase image conforms the fieldmap with a scale difference; the dipole effect manifests as bright and dark lobes as delimited by a conic zero surface at the magic angle. In large phase angle scenarios, a phase image may get wrapped. The combination of dipole effect and phase wrapping effect may intrigue the phase image in an appearance of noise and cluttering.

T2* phase image processing

As diagrammed in Figure 1, a large phase angle may cause a phase wrapping effect during the complex mapping (via $\exp(i\gamma b(x,y,z)T_E)$ for $|\gamma b(x,y,z)T_E| > \pi$). The phase wrapping effect is a conspicuous artifact due to a periodic nonlinear mapping, which manifests as contours in a T2* phase image.

The wrapped phase image can be unwrapped through a phase unwrapping procedure. The 3D phase unwrapping problem remains a challenge due to its complexity [20,21]. Recent research on MRI phase analysis [22,23] shows that the 3D MR phase unwrapping problem can be efficiently solved by a Laplacian technique with the implementation of Fourier transforms, which is

$$P[\mathbf{r}] = IFT \left\{ \frac{FT \left\{ \cos P^{raw} \cdot IFT \left(k^2 \cdot FT(\sin P^{raw}) \right) - \sin P^{raw} \cdot IFT \left(k^2 \cdot FT(\cos P^{raw}) \right) \right\}}{k^2} \right\}, \quad (9)$$

where P^{raw} denotes the raw phase image represented in a range of $[-\pi, \pi]$ in units of radian (usually wrapped) and $k = |\mathbf{k}|$ as the 3D discrete coordinates in the 3D Fourier domain. It is noted that in Eq. (9) the IFT and FT come into play in pairing, which can be efficiently computed. In practice, the Laplacian-based phase unwrapping algorithm in Eq (9) enables a real-time implementation; it not only achieves phase unwrapping, but also removes flat background and harmonic spatial components [22,24,25].

TVB algorithm for dipole inversion

We deal with the dipole inversion problem in Eq. (8) in the framework of 3D deconvolution image processing. Indeed, the dipole conversion is an unusual 3D deconvolution in that the bipolar-valued anisotropic kernel (in Figure 3) dooms a severely ill-posed inverse problem; for this we propose a solution by using a powerful 3D TVB [11,12]. The 3-subproblem split TVB algorithm is expressed by

$$\chi^{recon} = \min_{\mathbf{d}, v, \chi} \left\| \mathbf{d} \right\|_{TV}^2 + \frac{\lambda}{2} \left\| B_0 v - b^p \right\|_2^2 + \frac{\gamma_1}{2} \left\| \mathbf{d} - \nabla \chi - \mathbf{a}_1 \right\|_2^2 + \frac{\gamma_2}{2} \left\| v - h_0 * \chi - a_2 \right\|_2^2 \quad (10)$$

with $\mathbf{d} = \nabla \chi$ and $v = h_0 * \chi$

where the auxiliary parameters $\{\gamma_1', \gamma_2', \mathbf{a}_1', \mathbf{a}_2'\}$ are introduced for the split algorithm implementation and fast convergence.

In iteration implementation, the split 3-subproblems in Eq. (10) are solved one at a time (with respect to one of $\{\mathbf{d}', v', \chi'\}$ while keeping the other two fixed). The following input is required: 3D fieldmap b^p , 3D convolution kernel h , regularization parameter λ (adjustable), and convergence control tolerance of error (preset), and maximum iteration number allowed (preset). In summary, the TVB algorithm in Eq. (10) is implemented by the following pseudocode:

```

Initialize  $\chi=v=a_2=0, \mathbf{d}=0$ 

Do

    Minimization of  $\chi$ -subproblem with  $(\mathbf{d},v)$  fixed;

    Minimization of  $\mathbf{d}$ -subproblem with  $(\chi,v)$  fixed;

    Minimization of  $v$ -subproblem with  $(\chi,\mathbf{d})$  fixed;

    Update  $\mathbf{a}_1 := \mathbf{a}_1 + \nabla \chi - \mathbf{d}$ 

    Update  $a_2 := a_2 + h * \chi - v$ 

While "not converged"

```

In the result of iterative reconstruction, we obtain a discrete χ source map, $\chi^{\text{recon}}[x,y,z]$, which is a tomographic reconstruction of the true unknown continuous χ distribution inside an object. It is pointed out that we implement χ tomography by a linear two-step CIMRI model under linear approximations. The CIMRI reconstruction may suffer certain errors from T2* phase image processing and the inherent phase nonlinearity (in step 1 in Eq. (7)) and from incomplete dipole inversion (in step 2 in Eq. (10)).

RESULTS

Numerical simulations, phantom experiments, and human brain imaging experiments are presented in this section.

Numerical simulations

First, we performed a simple χ tomography simulation with a cylindrical χ source. The simple geometry of a cylinder has a well-established magnetostatic analytic formula [3,26] for fieldmap calculation. We predefined a cylindrical χ distribution in a cubic field of view (FOV), in a matrix of $128 \times 128 \times 128$, with the setting of $\chi = 1\text{ppm}$ (ppm: parts per million in SI unit) inside cylinder and $\chi = 0$ elsewhere. The χ -induced fieldmap in a main field ($B_0=3\text{T}$) was calculated by a 3D convolution in Eq. (1), with the cylinder axis perpendicular B_0 direction. An additive Gaussian noise was added to the fieldmap to simulate a noisy fieldmap. From the fieldmap, we reconstructed the χ map using the TVB algorithm. The simulation results are presented in Figure 4, which shows that the χ -induced fieldmap suffers from a conspicuous dipole effect, in a manifestation of bright and dark sheaths around the cylinder, and that the TVB could reliably remove the dipole effect in χ^{recon} from a single-angle fieldmap.

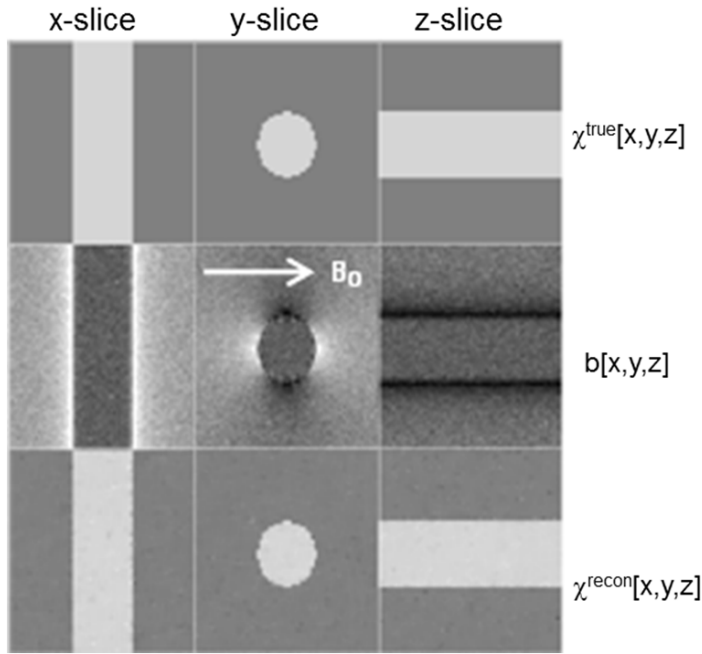


Figure 4: Numerical simulations of tomographic χ reconstruction with a cylindrical geometry.

Top row: a predefined 3D cylindrical χ distribution $\chi^{\text{true}}[x,y,z]$ (displayed at three principal orthogonal planes); middle row: the χ -induced fieldmap $b(x,y,z)$ calculated by a 3D convolution of χ^{true} with a dipole kernel (B_0 is perpendicular to cylinder axis); bottom row: a TVB-reconstructed χ map. A χ tomography implements an equality of $\chi^{\text{recon}}[x,y,z] = \chi^{\text{true}}[x,y,z]$ up to a certain noise. [12].

Next, we performed a 3D brain χ tomography with a digital brain χ phantom, as shown in Figure 5 (a1,b1,c1) with three principal orthogonal slices. The brain χ geometry consists of ellipsoids and Gaussian-shaped balls, as defined in a 3D volume in a normalized dimension of $[-0.5, 0.5] \times [-0.5, 0.5] \times [-0.5, 0.5]$ by the following formula:

$$\begin{aligned}
 V_0(x, y, z) &= \begin{cases} 1, & \left(\frac{x}{0.45}\right)^2 + \left(\frac{y}{0.33}\right)^2 + \left(\frac{z}{0.33}\right)^2 < 1 \\ 0, & \text{otherwise} \end{cases} \\
 V_1(x, y, z) &= \begin{cases} 1, & \left(\frac{x-0.25}{0.05}\right)^2 + \left(\frac{y}{0.03}\right)^2 + \left(\frac{z}{0.03}\right)^2 < 1 \\ 0, & \text{otherwise} \end{cases} \\
 V_2(x, y, z) &= \begin{cases} 1, & \left(\frac{x}{0.06}\right)^2 + \left(\frac{y}{0.03}\right)^2 + \left(\frac{z}{0.03}\right)^2 < 1 \\ 0, & \text{otherwise} \end{cases} \\
 V_3(x, y, z) &= \exp\left(-\left(\frac{x+0.16}{0.41}\right)^2 - \left(\frac{y-0.16}{0.21}\right)^2 - \left(\frac{z}{0.21}\right)^2\right) \\
 V_4(x, y, z) &= \exp\left(-\left(\frac{x+0.16}{0.41}\right)^2 - \left(\frac{y+0.16}{0.21}\right)^2 - \left(\frac{z}{0.21}\right)^2\right)
 \end{aligned} \quad . \quad (11)$$

The brain χ distribution is a combination of the geometrical primitives with an additive noise by the following formula:

$$\chi(x, y, z) = 0.2V_0 + 0.8V_1 - 0.5V_2 + 0.8V_3 + 0.8V_4 + \text{noise} \quad (12)$$

It is noted that the predefined χ source in Eq. (12) assumes a bipolar-valued distribution in a range of [-0.3, 1] ppm. The binary ellipsoids (V_0, V_1, V_2) provide sharp boundaries and the Gaussian-shaped balls (V_3, V_4) simulate local activation blobs with tapered edges. The T2*MRI simulation was done with the setting of $B_0 = 3\text{T}$, $T_E = 30\text{ms}$, FOV matrix: $128 \times 128 \times 128$). The simulation results are presented in Figure 5, which show that the T2* magnitude image suffers orientation effect, edge effect and negative inversion, and that the T2* phase image conforms with the χ -induced fieldmap (except for phase-wrapped regions), both suffering a conspicuous dipole effect. The TVB algorithm could remove any dipole effect, thereby reproducing the χ source map. Since only one phase image is used for χ source reconstruction, the simulations show that χ tomography can be reliably achieved from a single-angle phase image.

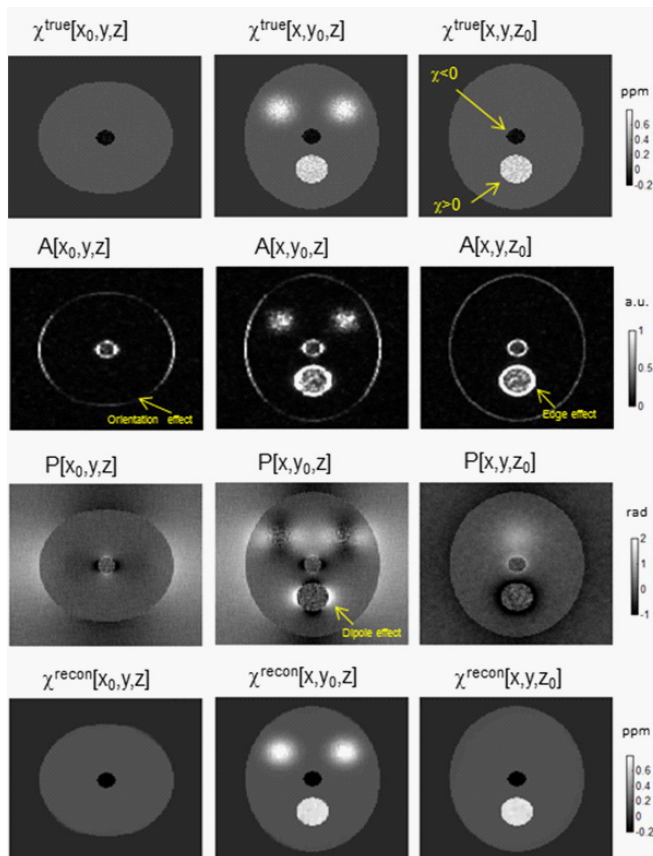


Figure 5: Numerical Simulations of T2*MRI and χ tomography with a brain phantom.

Top row: The 3D χ geometry of a digital brain phantom (displayed at three principal orthogonal planes); 2nd row: the 3D T2* magnitude image; 3rd row: the 3D T2* phase image; bottom row: the TVB-reconstructed χ map. The T2* magnitude suffers from nonnegativity, orientation effect, and edge effect. The T2* phase image suffers from dipole effect. A χ tomography implements an equality of $\chi^{\text{recon}}[x,y,z] = \chi^{\text{true}}[x,y,z]$ up to a certain noise.

Phantom Experiments

We performed a phantom experiment with a Gadolinium (Gd)-filled tube [27], as demonstrated in Figure 6. Specifically, Figure 6(a) shows the χ source phantom, which was a plastic tube filled with Gd contrast (dilution of Magnevist Gd dye) inserted in a large water tank. The tube phantom provides a uniform cylindrical χ distribution, a physical implementation of the digital cylinder phantom in Figure 4. Through a T2*MRI experiment (on a Siemens Trio 3T scanner with a GRE-EPI sequence, $T_E=30\text{ms}$, voxel size $3\times3\times3\text{ mm}^3$, FOV matrix: $128\times128\times64$, flipping angle= 75°), we obtained the T2* magnitude image (in Figure 6(b)) and the T2* phase image (in Figure 6(c)). From the T2* phase image, we reconstructed the χ source (in Figure 6(d)). It is seen that the reconstructed χ distribution takes on a uniform cross-section of the tube cylinder (ground truth).

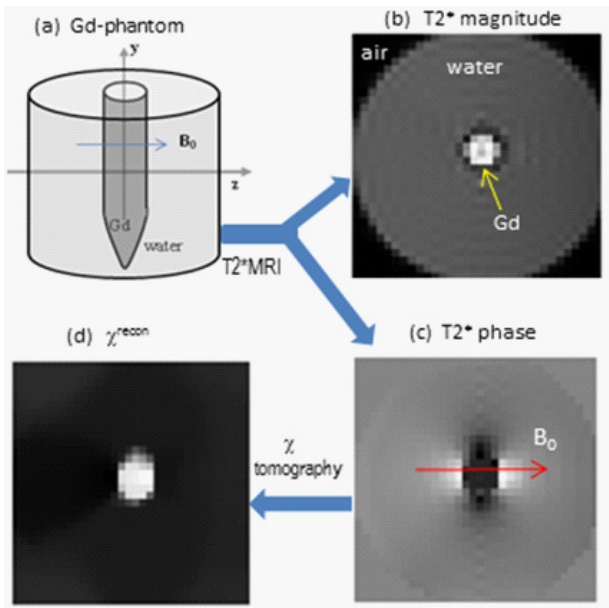


Figure 6: Phantom experiments with a Gd-filled tube.

(a) The geometry of Gd-filled tube phantom (a cylindrical χ distribution); (b) T2* magnitude (acquired by a GRE-EPI sequence); (c) T2* phase image (acquired by a GRE-EPI sequence); (d) a TVB-reconstructed χ map (a replica of a cross section of the cylindrical χ source) [27].

In vivo Human Brain Experiments

In Figure 7 is demonstrated a human brain imaging on a 3T Siemens TrioTim system for brain χ reconstruction, with the following experimental settings: $B_0 = 3\text{ T}$, GRE sequence, $T_E = 25\text{ms}$, flip angle = 75° , and voxel size is $0.5\times0.5\times1.5\text{ mm}^3$. It is seen that the raw T2* phase image was severely unwrapped. After phase unwrapping processing by Eq (9) and postprocessing, we obtained the fieldmap and reconstructed the χ map by CIMRI.

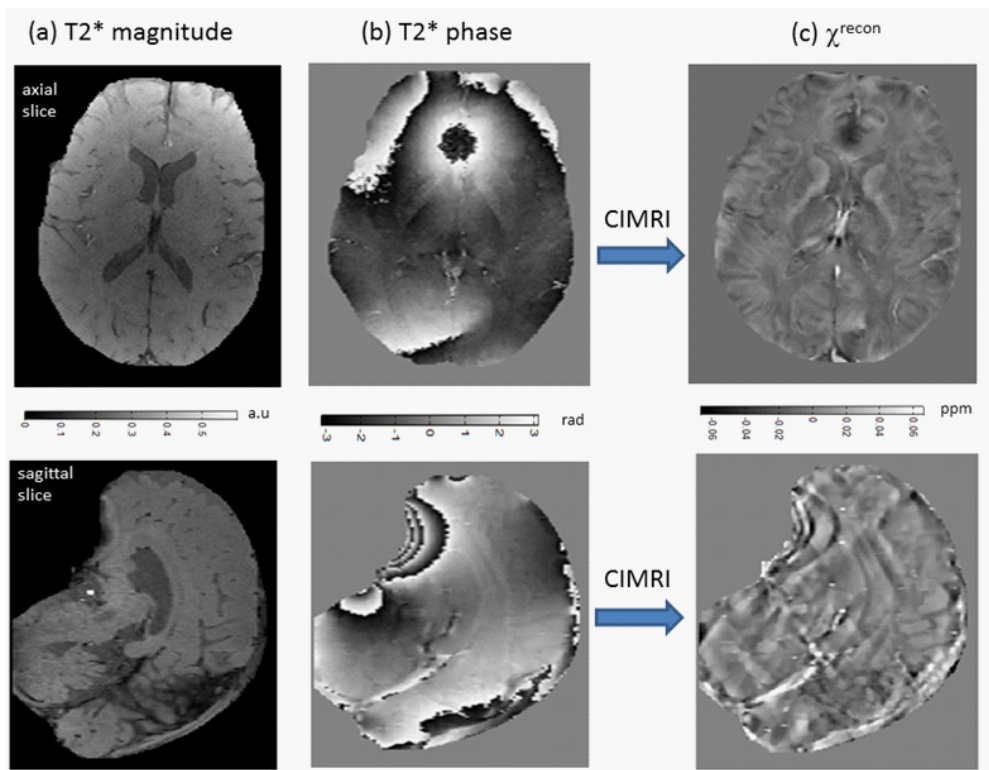


Figure 7. An *in vivo* human brain imaging experiment at a Siemens TrioTim 3T system with T2* image acquisition through the use of a GRE sequence.

Top row: (a) A T2* magnitude image, (b) a T2* phase image, and (c) a TVB-reconstructed map at an axial slices; bottom row: a T2* magnitude, a T2* phase image, and a TVB-reconstructed χ -map at a sagittal slice. The T2* phase image was subject to Laplacian phase unwrapping and high-pass filtering. The χ map was reconstructed from T2* phase image by a two-step CIMRI model.

In Figure 8 is another human brain functional imaging experiment on a 7T Magnetom System with the following experimental settings: $B_0 = 7\text{T}$, scanning with a GRE-EPI sequence, $T_E/T_R = 29/3000\text{ms}$, flip angle = 75° , and voxel size is $0.5 \times 0.5 \times 1.2\text{mm}^3$. Figure 8 shows a snapshot capture of the *in vivo* brain state in magnitude and phase images along with the reconstructed brain χ map. The phase unwrapping processing and χ reconstruction were done with the same programs as used in the 3T experiment in Figure 7. The high-resolution, high-field fMRI data provides structural details in the reconstruction χ map, which enables the spatial co-localization with the functional patterns.

It is mentioned that the ground truth of *in vivo* brain χ distribution is unknown. The reconstructed χ maps are considered as the replicas of the brain χ state in the context of brain χ tomography, which demands a systematic calibration on the reconstruction procedure with brain-tissue-equivalent phantoms.

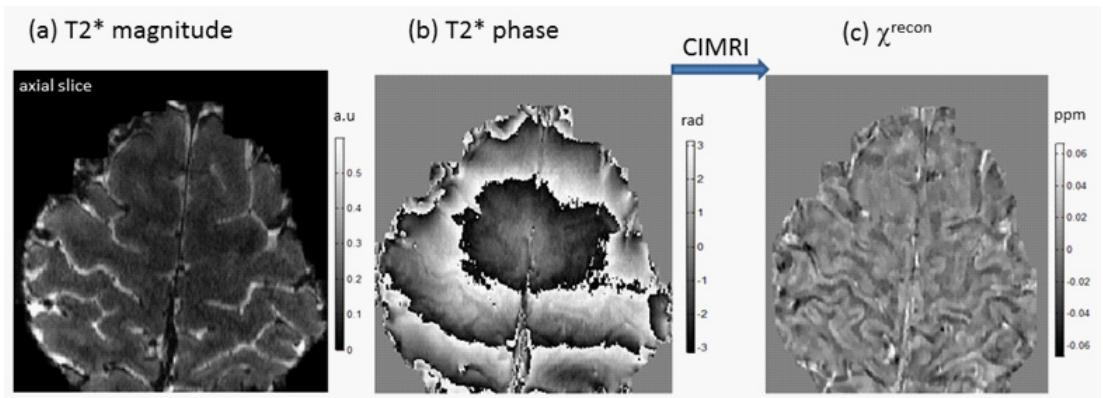


Figure 8: An *in vivo* human brain imaging experiment at a Siemens Magneto 7T system with T2* imaging by a EPI-GRE sequence.

The brain magnetic state was captured in a snapshot image of (a) magnitude and (b) phase (displayed with an axial slice). The tomographic χ reconstruction in (c) provides a brain χ map with details of sulci and gyri.

DISCUSSION AND CONCLUSION

MRI is considered a tomographic imaging method because it is capable of noninvasively depicting the material interior magnetic state with some empirical parameters (T1, T2, T2*). In MRI principle, the internal magnetic fieldmap is measured through the use of a carrier of hydrogen protons that sense the magnetic field in Larmor precessions, producing trigonometric spin precession signals. Therefore, the output of MRI is a complex-valued image in nature. A conventional MR image only exploits the magnitude component. A complex MRI model implements a tomographic reconstruction of the complex signal distribution (illustrated in the bottom box in Figure 1), but not the tomographic reconstruction of the internal χ source distribution or the internal fieldmap. That is, neither the MR magnitude nor the phase could be interpreted as a direct representation of the internal fieldmap or the χ source. We propose using the inverse MRI model for the χ source reconstruction, which is only applicable from the MR phase image but not feasible from the MR magnitude. In theory, χ tomography requires a small phase angle condition that is seldom satisfied in practice. In large phase angle scenarios, χ tomography may suffer certain errors (albeit weak) due to the imperfect phase unwrapping processing and the inherent phase nonlinearity (originated from trigonometric spin signal nonlinearity [10]).

MRI is a versatile imaging technology that acquires data through the use of a variety of pulse sequences with a protocol of parameter settings. In this report, we are concerned with the tomographic reconstruction of tissue χ mapping, the underlying magnetic source for T2* image; for which we address T2*MRI that uses a GRE sequence for data acquisition and its inverse model for χ source reconstruction. The concept of inverse T2*MRI may be extended to the inverse problems of T1- and T2-weighting mechanisms. For example, from the output of complex T2 images acquired through the use of a spin echo (SE) sequence, we may reconstruct an internal

fieldmap and a χ source map in the same way as is done for inverse T2*MRI. Since the static inhomogeneous fieldmap component has been suppressed by an SE sequence, the reconstructed χ map from a T2 phase image only represent the residual of dynamic randomness of tissue χ source (where the dynamic internal fieldmap is a transient distribution that is not refocusable by an SE sequence). The interpretation on the reconstructed T2 magnetic source by CIMRI remains unclear, which is an ongoing research topic.

A CIMRI-reconstructed multivoxel χ map is used to represent the true continuous χ source. Besides the discreteness error (governed by Shannon sampling theory), the reconstructed χ map may suffer errors from other causes: 1) nonlinearity phase unwrapping; 2) imperfect background removal; and 3) dipole inversion regularization. In principle, the data zeroing degeneracy associated with the “multiply by zero” operation at a conic surface proximity in a 3D fieldmap may be lifted through the use of a multi-angle dataset [28]. In practice, the multi-angle data acquisition is not always operable and the TVB iteration algorithm can accommodate a sparse entry lacuna. Our simulations (in Figure. 4 and 5, in reference [29]) show that the TVB algorithm can reliably reconstruct the X source from a single-angle data.

It is straightforward to extend the 3D tomography and 4D χ tomography by repeating the 3D χ tomography for each snapshot in a time series of data [30]. For brain imaging applications, the 3D χ tomography reproduces a brain χ source distribution that offers a more truthful depiction of a brain structural state; and the 4D χ tomography reconstructs a 4D χ dataspace that allows the more direct and truthful brain functional mapping. It is expected, with the MR images acquired from high-field and high-resolution MRI systems, that the χ tomography may improve the source reconstruction performance considerably due to high signal-to-noise ratio (B_0 increase), fast snapshot capture (T_E decrease), and low discrete error (voxel decrease).

It is mentioned that the χ tomography has been described by quantitative susceptibility mapping (QSM) [7, 24, 31, 32], which refers to quantitative χ map reconstruction from MR phase images. In the context of medical imaging, χ tomography is more informative than QSM. It not only connotes a distortion-free digital reproduction of (a spatially-conformed reproduction more than a quantitative mapping), but also specifies the approach by computationally solving an inverse imaging problem.

In summary, MRI is a versatile, non-invasive, internal imaging technology that provides different image representations for material interior magnetic states through the use of a diverse set of pulse sequences with a variety of protocols. A conventional MRI only exploits the magnitude of a complex-valued MR image, producing images for internal magnetic states with the contrasts on empirical parameters (T_1 , T_2 , T_2^*). In this report, we have examined the insights of T2*MRI that uses a GRE sequence for χ -caused signal detection, and show that neither an MR magnitude nor a phase could be a tomographic representation of the internal χ source distribution. Based on a two-step T2*MRI model and a two-step inverse T2*MRI model, we propose to reconstruct

the χ source distribution from T2* phase images using a linear CIMRI model. In conclusion, χ tomography is achievable by computationally solving an inverse T2*MRI problem. As a result of removal of MRI transformations (including dipole effect and complex-valued spatial mapping), χ tomography reproduces an internal magnetic χ distribution that is free from MRI transformations. The concept of inverse MRI will greatly inspire the MRI community in seeking the true magnetic source from transformed MRI data.

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