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An improved method for susceptibility and radius quantification of cylindrical objects from MRI

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Abstract

A new method is developed to measure the magnetic susceptibilities and radii of small cylinder-like objects at arbitrary orientations accurately. This method for most biological substances only requires a standard gradient echo sequence with one or two echo times, depending on the orientation of an object relative to the main magnetic field. For objects oriented at the magic angle, however, this method is not applicable. As a byproduct of this method, the cross-sectional area as well as signals inside and outside the object can be determined. The uncertainty of each measurement is estimated from the error propagation method. Partial volume, dephasing, and phase aliasing effects are naturally included in the equations of this method. A number of simulations, phantom, and pilot *in-vivo* human studies are carried out to validate the theory. When the maximal phase value at the boundary of a given cylindrical object is larger than 3 radians, and the phase inside the object is more than 1 radian, the susceptibility can be accurately quantified within 15%. The radius of the object can be determined to subpixel accuracy. This is the case when the signal-to-noise ratio inside the object is about 6:1 or higher and the radius of the object is about one pixel or larger. These conditions are realistic when considering medullary and pial veins for example.

Keywords

Magnetic moment; Susceptibility; Subpixel; Vein; Multi-echo gradient echo

1. Introduction

The magnetic susceptibility of *in-vivo* objects can reveal the property of the objects or physiological information. For example, the susceptibility of blood is affected by the oxygen saturation level [1–3]. Therefore, measuring oxygen saturation may provide important clinical diagnostic information. Several research groups [3–6] have tried to measure the susceptibility of blood. Lai et al. [4] and Langham et al. [5] have quantified the

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susceptibility of blood in large veins by using the phase information inside veins. On the other hand, Sedlacik et al. [6] has used a general fitting method to extract the size of a vein, its magnetic susceptibility, and other variables, from a 20-echo gradient echo MR sequence. As a result, the latter approach will require a much longer than usual scan time. Recently, the susceptibility of veins has been quantified by quantitative susceptibility mapping (QSM) techniques from different groups [7–20]. In general, QSM techniques may be divided into two major categories. One is an inverse method [9–15]. The other is a constrained regularization approach [15–20]. The inverse method may underestimate susceptibility values in small objects (whose diameters are less than 4 pixels) [11, 14, 16]. The constrained regularization approach may underestimate or overestimate the true susceptibility (as we will show later) and may take time to generate just one set of susceptibility maps. In addition, the intrinsic uncertainty of QSM methods has not been studied rigorously.

In this paper, we introduce a method that requires only one or two echo times from a standard gradient echo sequence for most *in-vivo* cylindrical objects and can quantify the susceptibility and cross-sectional area of a narrow cylinder for most orientations (except for the magic angle). For most biological tissues, as magnetic susceptibility of an object is roughly known in advance, using one or two echoes can significantly reduce the possible solutions of susceptibility values and obtain a unique answer. Our previous work [21] has demonstrated how to quantify the effective magnetic moment and susceptibility of a narrow cylinder, with no magnetic resonance (MR) signal inside the cylinder. This paper will focus on the quantifications of susceptibility and cross-sectional area from any given cylindrical object *with an MR signal*.

Our method relies on equations solved with known imaging parameters. In general, we quantify the following unknowns in sequence: orientation θ , effective magnetic moment $\mathcal{M}$, spin density outside the object ρ_0 , susceptibility χ , radius of the object a , and spin density of the object $\rho_{0,c}$. We only need three concentric circles around a given cylindrical object for these quantifications. We will review the complex signal induced from a cylinder in the next section. Section 2.2 shows how to systematically obtain the susceptibility and object size from a cylindrical object at an arbitrary orientation, except for the parallel ($\theta = 0^\circ$) and magic angle ($\theta = 54.7^\circ$) orientations. Section 2.3 explains how to solve the susceptibility of an object when it is parallel to the main field. The magic angle orientation will be discussed later in Section 2.4. Uncertainties of susceptibility and other unknowns will be studied through the error propagation method [22] in Section 2.5, and relevant formulas will be provided in Appendices A and B. Sections 2.6, 2.7, and 2.8 describe procedures and post-processing steps of our simulations, phantom, and human studies. Our results and comparisons to two QSM methods will be shown in Section 3. Factors affecting the accuracy and precision of susceptibility quantifications based on our method will be discussed in Sections 4.1 and 4.3. In addition, as multiple solutions of susceptibility from our equations may occur, we comment on how to reduce possible solutions in Section 4.2. Finally, we will discuss the limitations of our method and future work in Section 4.4.

2. Methods and materials

2.1. MR signal of a cylindrical volume containing a coaxial object

As we have previously described the theoretical concept of this signal calculation in [21], here we only summarize the concept and needed equations. We begin with the phase value of the complex MR signal inside an infinitely long cylinder (or a finite cylinder with a ratio of the height to the diameter being at least 5 to 1 [23]) from a gradient echo sequence [2]

$$\phi_{in} = -\gamma \frac{\Delta\chi}{6} (3 \cos^2\theta - 1) B_0 T_E \equiv \frac{g}{3} (1 - 3 \cos^2\theta) \quad (1)$$

where γ is the proton gyromagnetic ratio ($2\pi 42.58$) MHz/T, χ is the susceptibility difference between the regions inside and outside the object, θ is the angle between the main field direction and the axis of the cylinder (see Fig. 1a), B_0 is the main magnetic field, T_E is the echo time, and $g \equiv 0.5 \gamma B_0 \chi T_E$. The orientation θ can be estimated manually from a 3-dimensional (3D) data set based on the coordinates of the two end points of a cylindrical object. The word susceptibility hereafter refers to χ , unless it is otherwise explained. We have adopted the SI units throughout the paper.

The phase outside the cylindrical object is given by

$$\phi_{out} = -\gamma \Delta B T_E = -\gamma \frac{\Delta\chi a^2}{2 \rho^2} B_0 T_E \cos 2\psi \sin^2\theta \quad (2)$$

where ρ is the perpendicular distance measured from the axis of the cylinder, and ψ is the polar angle associated with ρ . A drawing depicting a cylindrical object and those angles is displayed in Fig. 1a.

Through choosing a coaxial pseudo-cylinder of radius R , which is around the cylindrical object of interest with a radius of a (such that $R > a$ shown in Fig. 1b), the overall gradient echo signal within R from a slice perpendicular to the axis of the cylinder is given by

$$S = \ell \rho_0 \int_a^R d\rho \rho \int_0^{2\pi} d\psi e^{i\phi_{out}} + \pi \ell a^2 \rho_{0,c} e^{i\phi_{in}} \quad (3)$$

$$= \pi \ell \rho_0 \int_{\varphi/R^2}^{g'} \frac{dx}{x^2} J_0(x) + \pi \ell a^2 \rho_{0,c} e^{i\phi_{in}} \quad (4)$$

where ℓ is the slice thickness of the image or can be an arbitrary length of the cylindrical object, ρ_0 is the effective spin density outside the object, $\rho_{0,c}$ is the effective spin density inside the cylindrical object, $\mathcal{P}$ is the effective magnetic moment defined by $\mathcal{P} \equiv g a^2 \cdot \sin^2\theta \equiv g' a^2$, g' is the maximal (or minimal) phase value at the surface of the object (see Eq. (2)) and is defined by $g' \equiv g \cdot \sin^2\theta$, and J_0 is the zeroth order Bessel function. The word “effective” is dropped from this point on. Both $\rho_{0,c}$ and ρ_0 are treated as unknown constants in Eq. (4) and they depend on imaging parameters, actual spin densities, and relaxation times T_1 and T_2 .

2.2. Susceptibility quantification of a cylindrical object with MR signal

Eq. (4) contains four independent unknowns: the magnetic moment, susceptibility, and two spin densities (i.e., ρ_0 and $\rho_{0,c}$). We first choose one circle to determine the center of the object. The center of the object as shown in Fig. 1b can be identified by minimizing the real part of the overall signal from a circle enclosing the cross section of the object (see Section 3.1 of [21]). As the signals are added within the circle, this procedure of finding the center of the object is minimally affected by the partial volume effect or any subpixel shift of the center. After identifying the center of the object, we choose three concentric circles to quantify the magnetic moment $\mathcal{P}$. Fig. 1b shows the schematic drawing of the three radii (R_1, R_2, R_3) for the magnetic moment quantification. The optimal choices of those radii have been described in [21]. Briefly, from Eq. (4), we can derive

$$Re(S_1 - S_2) \int_{\varphi/R_2^2}^{\varphi/R_3^2} \frac{dx}{x^2} J_0(x) = Re(S_2 - S_3) \int_{\varphi/R_1^2}^{\varphi/R_2^2} \frac{dx}{x^2} J_0(x) \quad (5)$$

where S_1, S_2 , and S_3 are calculated from complex sums of the signals (from images) enclosed by R_1, R_2 , and R_3 , respectively, and $R_1 > R_2 > R_3$. In addition, $Re(S)$ is the real part of the complex signal S . Note that $\mathcal{P}$ is the only unknown in Eq. (5) to be solved. On the other hand, both $\pm \mathcal{P}$ satisfy Eq. (5). In order to improve the accuracy of our measurements of those complex sums, each image pixel is further divided into 100 subpixels, as explained in [24].

After finding $\mathcal{P}$, we can solve the spin density outside the object (ρ_0) from two concentric circles in the following equation, derived from Eq. (4).

$$Re(S_1 - S_2) = \pi \ell \rho_0 \mathcal{P} \int_{\varphi/R_1^2}^{\varphi/R_2^2} \frac{dx}{x^2} J_0(x) \quad (6)$$

Here we choose the annular region between R_1 and R_2 , as this region contains more pixels than those between R_2 and R_3 .

We can now proceed to solve χ . By eliminating $\pi \ell a^2 \rho_{0,c}$ in Eq. (4), the complex signal S can be rewritten into one equation, in which susceptibility χ is the only unknown.

$$Re(S) \sin \phi_{in} = Im(S) \cos \phi_{in} + \pi \ell \rho_0 \mathcal{P} \sin \phi_{in} \int_{\varphi/R_2^2}^{\varphi/R_1^2} \frac{dx}{x^2} J_0(x) = Im(S) \cos \phi_{in} + \pi \ell \rho_0 |\mathcal{P}| \sin \phi_{in} \int_{|\varphi|/R_2^2}^{|\varphi|/R_1^2} \frac{dx}{x^2} J_0(x) \quad (7)$$

where $Im(S)$ is the imaginary part of the complex signal S . After the susceptibility is solved from the Van Wijngaarden–Dekker–Brent method [25], the radius a of the object can be calculated from $\sqrt{\varphi/g'}$. For our quantifications, we choose $R = R_3$, which is the innermost radius shown in Fig. 1b, and its corresponding $S = S_3$ for Eq. (7). The sign of the susceptibility solved from Eq. (7) will indicate whether the object is paramagnetic or diamagnetic relative to its surrounding environment, if the counterclockwise definition of the spin rotation [26] is used as in Eqs. (1) and (2). If a vendor uses the clockwise definition, then the susceptibility solved from Eq. (7) should be multiplied by a minus sign. Afterward, Eq. (4) will allow us to solve $\rho_{0,c}$. It is important to note that due to the nonlinear nature of

Eq. (7), multiple solutions of the susceptibility may exist. This will depend on the value of g' and this is further discussed in detail in Sections 4.2 and Appendix C.

2.3. A cylindrical object parallel to the main field

To be more general, the descriptions in this subsection include orientations of objects close to 0° . These situations have little phase distributions outside those objects and the above approach becomes unpractical, due to very small or nulled ϕ . In addition, phase inside a small object may be aliased and also affected by the Gibbs ringing. Thus, we utilize the complex signals at two different echo times to solve for χ . We then solve for radius a . The details are described below. First, we quantify spin density outside the cylinder of interest with two concentric circles at each echo time. When θ is close to 0° , we can assume that $|g'|$ is less than 1 with some choices of T_E . In the condition of $|g'| < 1$, $J_0(x)$ can be well approximated by $1 - x^2/4$ and Eq. (7) can be rewritten as

$$Re(S_n) \sin \phi_{in,n} = Im(S_n) \cos \phi_{in,n} + \pi \ell \rho_{0,n} \sin \phi_{in,n} \left(R^2 + \frac{g_n'^2 a^4}{4R^2} - a^2 - \frac{g_n'^2 a^2}{4} \right) \quad (8)$$

where the subscript n is referred to each variable obtained at the n^{th} echo time $T_{E,n}$, as those variables depend on the echo time. At each echo time, if we choose two different radii, $R_a > a$ and $R_b > a$, then we can derive

$$Re(S_{n,a}) - Re(S_{n,b}) = \pi \ell \rho_{0,n} (R_a^2 - R_b^2) \left(1 - \frac{g_n'^2 a^4}{4R_a^2 R_b^2} \right) \quad (9)$$

As $|\phi_n|/R^2 = |g_n'|a^2/R^2$ and is the maximal phase at radius R , with the presumptive $|g_n'| < 1$, it will be easy enough to choose slightly large R_a and R_b such that both $|g_n'|a^2/R_a^2$ and $|g_n'|a^2/R_b^2$ are less than 0.5. This will lead to $(g_n'^2 a^4) / (4R_a^2 R_b^2) < 1/16$, which can be neglected from Eq. (9). As a result, each $\rho_{0,n}$ can be estimated from Eq. (9).

Furthermore, if we choose the same R on images at two different echo times T_{E_1} and T_{E_2} , then Eq. (8) can be rewritten as

$$Re(S_1) \sin \phi_{in,1} = Im(S_1) \cos \phi_{in,1} + \pi \ell \rho_{0,1} \sin \phi_{in,1} \left(R^2 + \frac{g_1'^2 a^4}{4R^2} - a^2 - \frac{g_1'^2 a^2}{4} \right) \quad (10)$$

$$Re(S_2) \sin \phi_{in,2} = Im(S_2) \cos \phi_{in,2} + \pi \ell \rho_{0,2} \sin \phi_{in,2} \left(R^2 + \frac{g_2'^2 a^4}{4R^2} - a^2 - \frac{g_2'^2 a^2}{4} \right) \quad (11)$$

By multiplying Eq. (10) by $\rho_{0,2} \sin \phi_{in,2}$ and multiplying Eq. (11) by $\rho_{0,1} \sin \phi_{in,1}$, we obtain

$$\begin{aligned} (\rho_{0,2} Re(S_1) - \rho_{0,1} Re(S_2)) \sin(\phi_{in,1}) \sin(\phi_{in,2}) &= \pi \ell \rho_{0,1} \rho_{0,2} \sin(\phi_{in,1}) \sin(\phi_{in,2}) \frac{a^2}{4} \left(1 - \frac{a^2}{R^2} \right) (g_2'^2 - g_1'^2) \\ &+ \rho_{0,2} Im(S_1) \sin(\phi_{in,2}) \cos(\phi_{in,1}) - \rho_{0,1} Im(S_2) \sin(\phi_{in,1}) \cos(\phi_{in,2}) \end{aligned} \quad (12)$$

Eq. (12) now contains only two unknowns: the radius of the object a and the magnetic susceptibility χ . When the orientation is close to 0° , we may neglect the g'^2 term in Eq.

(12) and χ becomes the only unknown in the equation. As $\phi_{in}(T_{E_n}) \simeq -2g_n/3$, Eq. (12) becomes

$$\begin{aligned} & \left[\rho_{0,2} \text{Im}(S_{T_{E_1}}) + \rho_{0,1} \text{Im}(S_{T_{E_2}}) \right] \sin\left(\frac{2(g_1 - g_2)}{3}\right) - \left[\rho_{0,2} \text{Im}(S_{T_{E_1}}) - \rho_{0,1} \text{Im}(S_{T_{E_2}}) \right] \sin\left(\frac{2(g_1 + g_2)}{3}\right) \\ & = \left[\rho_{0,2} \text{Re}(S_{T_{E_1}}) - \rho_{0,1} \text{Re}(S_{T_{E_2}}) \right] \left[\cos\left(\frac{2(g_1 - g_2)}{3}\right) - \cos\left(\frac{2(g_1 + g_2)}{3}\right) \right] \end{aligned} \quad (13)$$

After solving χ , the cross-sectional area of the object, πa^2 , can be solved from Eq. (8) and $\rho_{0,c}$ can be uniquely solved from the imaginary part $\text{Im}(S) = \pi \ell a^2 \rho_{0,c} \sin \phi_{in}$ of the object signal.

The nature of trigonometric functions may lead to multiple solutions of χ . However, those solutions should be validated by checking whether they satisfy both Eqs. (10) and (11). In addition, as almost all biological tissues have $|\chi| \leq 2$ ppm [27], for $B_0 = 3$ T and $T_E = 11.7$ ms, these values lead to $|\phi_{in}| \leq 2\pi$. If $|g'|$ is small but not zero, then based on discussions in Appendix C.2 and knowledge of the signs of $\text{Im}(S)$ from summation and ϕ_{in} from a direct measurement of phase images, the possible number of solutions of susceptibility for a biological tissue with the stated MR parameters is no more than two. If $g' = 0$, we can either estimate the radius a of the object or neglect it in Eq. (8), and then follow a similar approach described in Appendix C.1 to solve the susceptibility. In this scenario, the solved ϕ_{in} is unique between 0 and 2π . If two or more solutions simultaneously satisfy Eqs. (10) and (11), then more echo times can be used to determine the actual solution of χ . More details are discussed in Section 4.2.

2.4. The magic angle orientation

When the orientation of a cylindrical object is close to the magic angle, phase inside the object is zero, and the second term (the complex term) in Eq. (4) becomes a real number. In this orientation, the single echo approach is not applicable, as the signal inside the object does not produce an imaginary part. As a result, the uncertainty of the susceptibility based on Eq. (A.1) becomes infinite. If we consider a double echo approach, with a short separation between two echoes such that $\rho_{0,c}$ does not vary too much between the two echo times, the signal difference between two echo times is roughly

$$S_{T_{E_1}} - S_{T_{E_2}} \approx \pi \ell \rho_{0,1} \wp_1 \int_{\varphi_1/R^2}^{g'_1} dx J_0(x) / x^2 - \pi \ell \rho_{0,2} \wp_2 \int_{\varphi_2/R^2}^{g'_2} dx J_0(x) / x^2 \quad (14)$$

where the subscripts 1 and 2 refer to the variables at the two echo times. As the magnetic moment and spin density outside the cylinder at two different echo times can be solved [21], Eq. (14) is again left with only one unknown, χ , to be solved.

In order to evaluate the feasibility of this approach, we have simulated images with a cylindrical object at the magic angle orientation and with imaging parameters given in Section 2.6.

2.5. Calculating uncertainties of susceptibility and other unknowns

The two major independent errors leading to uncertainties in susceptibility and other measures available in this work are from the thermal (white) noise due to the presence of the object and the systematic noise due to discrete pixels, partial volume, and Gibbs ringing in images. We can derive the uncertainty of χ based on Eq. (7) for most orientations or Eq. (12) for the parallel orientation, through the error propagation method [22]. Similarly, the uncertainties of object size and spin densities can be derived. These results are given in Appendices A and B. All noise estimates in Appendices A and B, including the orientation measurements, are uncorrelated. The minimization of uncertainties may also reveal the optimal imaging parameters or radius selection.

The thermal noise within an area A_R can be approximated by $\sigma \ell \sqrt{\Delta x \Delta y A_R}$, where σ is the standard deviation of the thermal noise in the images and Δx and Δy are the in-plane resolutions [24]. The error due to the systematic noise can be calculated if the center of the cylindrical object, the radius of the object, and the susceptibility difference are all known. Simulations and results of the systematic error have been discussed in [21, 24].

2.6. Simulations

In our simulations, we assumed a χ of 0.5 ppm and a main field of 3 T. We simulated each cylindrical object and its induced magnetic field on a 4096×4096 matrix and converted the matrix to 256×256 . We added the white noise to the 256×256 matrix. The detailed procedures were described in [21, 24]. We performed most of our simulations and susceptibility quantifications on a Pentium 4 personal computer. The radius of each cylindrical object on the 256×256 matrix was targeted to be one pixel. We simulated objects at five orientations $\theta = 90^\circ, 70^\circ, 57^\circ$ (magic angle), 40° , and 0° , and at three echo times $T_E = 11, 17$, and 20 ms. An effective spin density of 20 arbitrary units at $T_E = 0$ with a transverse relaxation rate, $R_2 = 10 \text{ s}^{-1}$, was used for the signal inside the cylinder but 10 for the outside. The standard deviation of the thermal noise (σ) was set to be one arbitrary unit such that the signal-to-noise ratio (SNR) outside the cylinder was 10:1. The complex signal from the innermost circle (see Fig. 1b) was utilized for the susceptibility quantification.

Liu et al. [28] and Liu et al. [29] suggested that more precise susceptibility values may be calculated from magnetic moments estimated from QSM. Thus, as a comparison between our method and QSM, we applied two QSM methods, susceptibility weighted imaging and mapping (SWIM) [11] and morphology enabled dipole inversion (MEDI) [17], to the same simulated images with the object at an orientation of 90° . For SWIM and MEDI, we duplicated each image 63 times in order to generate a 3D dataset for susceptibility quantification. We downloaded MEDI from <http://weill.cornell.edu/mri/pages/qsm.html> and tested it with the susceptibility quantification of an infinitely long cylinder with a radius of 16 pixels. The quantified susceptibility value perfectly matched with the input susceptibility value in this particular simulation.

2.7. Phantom studies

We prepared a gelatin solution with 60 g of gelatin powder in 1200 ml distilled water. We poured 800 ml of the gelatin solution into a rectangular plastic container, which has a length of 15.0 cm, width of 10.0 cm, and height of 14.0 cm. This was the body of our gel phantom. We prepared a gadolinium solution by adding 1.3 ml of the original Gd-DTPA (Gadolinium-diethylenetriaminepentacetate) magnetic resonance imaging (MRI) contrast agent (which has a concentration of 0.5 M) into the remaining 400 ml of the gelatin solution. The total volume of the gadolinium solution became 401.3 ml. We filled a 10.5 cm long empty straw with the gadolinium solution. We sealed both ends of the straw after it was filled. We immersed the filled straw completely into the middle of the gel phantom. A plastic stand holding up the straw was at the straw's bottom. The molar susceptibility of Gd-DTPA $\chi_{M,Gd-DTPA}$ is $4\pi \times (0.027 \pm 0.001)$ ppm/mM [3]. With water susceptibility roughly -9.05 ppm, the absolute volume susceptibility of the gadolinium solution was about -8.47 ± 0.05 ppm. The susceptibility of interest, χ , was therefore 0.58 ± 0.05 ppm. The diameter of the straw was 4.92 ± 0.02 mm, measured by a Vernier caliper, and it led to a cross-sectional area of 19.0 ± 0.2 mm².

We imaged the phantom with a conventional single-echo 3D spoiled gradient echo (SPGR) sequence, in a 3 T clinical GE Discovery MR750 machine. We used a quadrature head coil for all phantom studies. The imaging parameters were: $T_E = 11$ ms, 17 ms, and 20 ms, $T_R = 30$ ms, flip angle = 20° , read bandwidth = 244.14 Hz/pixel, resolution = 1 mm $\times$ 1 mm $\times$ 1 mm, and fields of view = 256 mm $\times$ 256 mm $\times$ 28 mm. We manually changed the echo time three times and acquired images from three echoes. The acquisition time for each echo was about 4 minutes. We rotated the entire phantom including the straw and scanned the phantom in four different orientations relative to the main field. We aligned images such that they were roughly perpendicular to the straw. As a result, the normal vector of the imaging plane with respect to the main field and the unit vector of the straw relative to the normal vector of the images were used to further determine the actual orientations of the straw with respect to the main field more accurately. The information of unit vectors was listed at tag numbers (0020, 0032) and (0020, 0037) in the DICOM header [30]. The actual orientations of the straw were determined to be roughly 90° , 75.5° , 28.2° , and 0° . We analyzed two different slices from each orientation and each echo time, in order to check the consistency in our phantom studies.

2.7.1. Steps to obtain susceptibility values—With the actual orientation of each straw measured from the procedures described above, the steps to obtain quantified susceptibility χ were as follows:

1. We collected and reconstructed the k-space data.
2. We manually unwrap the background phase in each phase image at each echo time by adding proper multiples of 2π in each aliased phase region.
3. We removed the background phase around each straw in each image from the following procedures. We first selected a region of interest (ROI) with a matrix size of 62×62 pixels centered around the straw of interest. We excluded pixels within a radius between 8 and 10 pixels around the straw, depending on the extent of the

dipolar phase pattern. We then fit a second order polynomial in 2D to the phase values of those remaining pixels in the ROI. The fitted polynomial from each image of interest represented the background phase, which was subtracted from the unwrapped phase image. A cleaned phase image was then obtained. On each cleaned phase image, the mean phase value from pixels inside the ROI but outside the dipolar phase pattern of the straw was close to zero. An example of the magnitude and cleaned phase image of the Gd-DPTA doped straw is shown in Fig. 2a and b.

4. After these procedures, we identified the center of the object (i.e., straw) with the searching algorithm described in [21].
5. With the known center of the object, we solved the magnetic moment of the object with Eq. (5) and the spin density surrounding the object with Eq. (6).
6. With the known orientation of the object, we solved the susceptibility of the object at each echo time with Eq. (7), for all orientations except for the parallel cases. For the parallel orientation, we solved the susceptibility of the object with Eq. (12) using two echo times.

To study the effect due to different straw sizes, we reduced the image resolutions of cleaned images and then applied our method for susceptibility quantifications. For each image of interest with the original size of 256×256 , we Fourier transformed the magnitude and cleaned phase images to k-space. Then we selected the central 128×128 or 100×100 points out of the 256×256 complex matrix in k-space. We inverse Fourier transformed those smaller matrices back to the image domain and obtained images with lower resolutions. As a result, the theoretical diameters of the straw became 2.46 ± 0.02 mm and 1.92 ± 0.02 mm, respectively. By doing this, we could evaluate our method in a consistent way without introducing additional experimental errors (e.g., effects due to the wall of a small straw).

We also applied SWIM and MEDI on the same cleaned phase images of matrix size 256×256 and 128×128 (but duplicated each image 63 times to generate a 3D dataset) at the 90° orientation. After obtaining the susceptibility maps from SWIM and MEDI, we calculated the mean and standard deviation of the susceptibility from four pixels completely inside the straw and from the central image of each 3D set. In addition, we also measured the background susceptibility values surrounding the straw. The susceptibility values quantified from SWIM and MEDI are shown in Table 5.

2.8. Pilot in-vivo study

A set of 3D gradient echo images of a female volunteer acquired from a 4 T Bruker/Siemens machine was available to us. The imaging parameters of the gradient echo sequence were $T_E = 19.2$ ms, $T_R = 26$ ms, flip angle = 11° , read bandwidth = 120 Hz/pixel, resolution = 0.5 mm $\times$ 0.5 mm $\times$ 0.51 mm, and field of view = 256 mm $\times$ 176 mm $\times$ 45 mm. We analyzed a vein on the transverse plane, as shown in Fig. 3a and b. The coronal and sagittal views of this vein are shown in Fig. 4. Fig. 4c shows a reasonable dipolar pattern of the vein in the phase image and no other objects around this vessel. We quantified the susceptibility with

the same steps described in the previous subsection, except that we removed the background phase with a 16×16 high pass filter. In addition to our method, we also applied SWIM to this *in-vivo* dataset and compared the susceptibility values between the two methods.

3. Results

We summarize below the quantified susceptibility values, cross-sectional areas (A_0), and spin densities from simulations and phantom studies for different orientations and echo times. In order to calculate the uncertainty of each measurement, we first need to estimate the uncertainties of the orientation and magnetic moment. The former is roughly one degree in all of our phantom studies while the latter is given in a formula shown in [21].

3.1. Arbitrary orientations except for the parallel orientation: simulations and phantom studies

3.1.1. Simulated images at 90°, 70°, and 40°—As shown in Table 1, most measurements of the susceptibility from our approach are close to the original input χ of 0.5 ppm. The differences between all quantified susceptibilities and the actual value are no more than 16%. On the other hand, the estimated uncertainties are sometimes larger due to smaller orientations and shorter echo times. The actual cross-sectional area of each simulated cylinder is 3.14 pixel^2 and the actual spin densities are 17.9, 16.9, and 16.4 at $T_E = 11, 17, \text{ and } 20 \text{ ms}$, respectively. The cross-sectional areas and spin densities solved from our approach agree with these true values to within 30%. Again, the estimated uncertainties can be even larger due to uncertainties propagated from susceptibility quantifications. Due to the combination of Gibbs ringing and finite sampling effects, the spin density values inside the objects have been systematically underestimated, as shown in Table 1. On the other hand, the spin densities outside the objects have been systematically overestimated.

3.1.2. Applications of SWIM and MEDI to simulated images—The magnetic moments and susceptibility values quantified from SWIM are $3.84 \text{ rad} \cdot \text{pixel}^2$ (0.87 ppm), $2.87 \text{ rad} \cdot \text{pixel}^2$ (0.42 ppm), and $2.89 \text{ rad} \cdot \text{pixel}^2$ (0.36 ppm) at $T_E = 11, 17, \text{ and } 20 \text{ ms}$, respectively. The magnetic moments and susceptibility values quantified from MEDI are $1.68 \text{ rad} \cdot \text{pixel}^2$ (0.38 ppm), $4.03 \text{ rad} \cdot \text{pixel}^2$ (0.59 ppm), and $5.30 \text{ rad} \cdot \text{pixel}^2$ (0.66 ppm) at $T_E = 11, 17, \text{ and } 20 \text{ ms}$, respectively. These results are not self consistent and they are at least 16% deviated away from the actual susceptibility value (0.5 ppm).

3.1.3. Simulated images at 57° (magic angle)—The quantified magnetic moments are $1.92 \pm 0.35 \text{ rad} \cdot \text{pixel}^2$, $2.58 \pm 0.23 \text{ rad} \cdot \text{pixel}^2$, and $2.98 \pm 0.21 \text{ rad} \cdot \text{pixel}^2$, at echo times 11, 17, and 20 ms, respectively. The quantified magnetic susceptibility is $0.80 \pm 3.20 \text{ ppm}$ obtained from $T_E = 11 \text{ ms}$ and 17 ms using Eq. (14). Similarly, the susceptibility value is $0.60 \pm 0.25 \text{ ppm}$ obtained from $T_E = 17 \text{ ms}$ and 20 ms. These results are quite different from the actual susceptibility 0.5 ppm. In addition, uncertainties derived from the error propagation method are fairly large. In general, when no phase value exists inside the object, eliminating the object signal as shown in Eq. (14) leads to large uncertainties of quantified susceptibilities. One alternative solution to this problem is to physically rotate the object by a certain angle even as small as 15° , in order to gain some signals of the imaginary part.

3.1.4. Phantom studies at three resolutions (matrix sizes)—Most of the susceptibilities measured from our method agree well within 12% of the theoretical value, 0.58 ± 0.05 ppm, for all orientations, different echo times, and image resolutions. The results are listed in Tables 2, 3, and 4. However, the quantified susceptibility values from the 100×100 matrix at angle 28.2° are not reliable. The measured cross-sectional areas and the theoretical value agree within 16%, except for results from the 28.2° orientation and from lower image resolutions. Some uncertainties are large due to large uncertainties propagated from the magnetic moments.

3.1.5. Applications of SWIM and MEDI to phantom studies—The susceptibility values quantified from SWIM and MEDI for phantom studies are listed in Table 5. For SWIM, we have assigned the suggested thresholding parameter 0.1 as well as other thresholding parameters 0.02 and 0.3 [11]. The susceptibility result using the thresholding parameter 0.02 is 0.40 ppm, but the map contains severe streak artifacts surrounding the straw filled with the gadolinium solution. The susceptibility result using the thresholding parameter 0.3 is 0.23 ppm. For the MEDI method, we have assigned regularization parameters, 50, 100, 250, 400, and 1000 into the kernel. The mean quantified susceptibility values from pixels inside the straw with different regularization parameters are identical to those listed in Table 5. All quantified susceptibility values from SWIM or MEDI are underestimated by at least 20% for the perpendicular orientation. For this reason, we do not quantify susceptibility values from SWIM or MEDI from any other orientations, as we expect worse results for those situations. These phantom and simulated results indicate that current SWIM or MEDI may not accurately quantify susceptibility from cylindrical objects with diameters of less than 5 pixels.

3.2. Parallel orientation: simulations and phantom studies

Results of simulations and phantom studies for the parallel orientation are shown in Tables 6, 7, 8, and 9. Each susceptibility was estimated from Eq. (13) with complex signals calculated from two echo times. In Table 6, a combination of $T_E = 11$ ms and 17 ms and $T_E = 17$ ms and 20 ms was used for susceptibility quantifications. In Table 7, a combination of $T_E = 11$ ms and 17 ms and $T_E = 11$ ms and 20 ms was used for susceptibility quantifications. The reasons for choosing these echo time combinations will be discussed in Section 4.3. The cross-sectional area of the object, the spin density around and outside the object, and the spin density inside the object were obtained at each echo time. All quantified susceptibility values agree well with the theoretical values. The differences between the quantified susceptibilities and the actual value in simulations were less than 2% and the differences between the quantified cross-sectional areas and the actual value were less than 8%. In phantom studies, the differences between the quantified susceptibilities and the theoretical value were less than 6%. The differences between quantified cross-sectional areas and the actual value were within 16% for most cases. At $T_E = 20$ ms, the estimated uncertainties of cross-sectional areas were very large. This will be discussed further in Section 4.3.

3.3. Pilot in-vivo study

By using our method, the measured magnetic moment of the vein in Fig. 4 is 2.13 rad-pixel^2 , its susceptibility value is 0.43 ppm, and its cross-sectional area is 1.58 pixel^2 . This

susceptibility value agrees with the expected susceptibility 0.40 ppm, if we assume an oxygenation level of 70%, a hematocrit of 0.4, and a susceptibility difference between the fully deoxygenated blood and fully oxygenated blood of 3.39 ppm [31]. As the signal inside the measured vein is about 130 units and the noise of images is about 27 units, the SNR of this vein is around 5 to 1. The SNR of the tissue outside the vein is about 8 to 1. On the other hand, the mean susceptibility value of this vein quantified from SWIM is 0.24 ppm. This pilot study demonstrates that our method will be feasible to clinical studies in the future.

4. Discussion

The magnetic moment, the signal of the object itself, and the orientation of the object are the three major factors affecting the quantification of susceptibility in our method.

Understanding their uncertainties and roles in the equations sheds some light on how one might improve the accuracy and precision of susceptibility quantifications.

4.1. Major factors affecting uncertainty for susceptibility quantification

4.1.1. Uncertainties of the measurements—The uncertainties of susceptibility and other variables are derived from the error propagation method (see Section 2.5). In order to reduce the uncertainty of a quantified susceptibility, the B^2 and C^2 term in Eq. (A.1) indicate that the radius of R_3 should not be chosen too large. This is to ensure that $Im(S_3)$ is above the noise level. On the other hand, R_3 cannot be too small either, as Gibbs ringing or partial volume can affect each measurement. We suggest R_3 to be at least 0.5 pixel away from the surface of the object but as small as possible. In addition, when $|g'|$ is larger than 3 radians and R_1 and R_2 are optimally chosen, it seems that B^2 and C^2 are the dominant terms in the numerator of Eq. (A.1).

If the susceptibility of an object is roughly known and the focus is to reduce the uncertainty of the measurement, as $\sin \phi_{in}$ appears in both denominator and numerator of Eq. (A.1), it may be helpful to increase the echo time such that $|\sin \phi_{in}|$ becomes unity. If this is not feasible, then one can try to increase the echo time such that $|g'|$ will be between 2.4 and 5.5, with $|g'| \approx 3.5$ being the optimal choice. This is because in this case, $J_0(g')$ becomes negative in the denominator of Eq. (A.1) and thus the uncertainty of susceptibility is reduced.

4.1.2. Signal inside the cylinder of interest—Eq. (A.1) indicates that increasing SNR inside the cylindrical object ($SNR_{0,c} = \rho_{0,c}/\sigma$) can reduce the uncertainty of quantified susceptibility. For a sufficiently long cylinder, SNR can be increased by using a thicker slice for example. Increasing the number of acquisitions is also an option, but at the expense of imaging time. In addition, a contrast agent may be used to increase the SNR of the object (e.g., vein). However, the use of contrast agent will mainly help to quantify the object radius more accurately but not to quantify the susceptibility of the object. Nonetheless, a pre- and post-contrast *in vivo* protocol may first allow the determination of the size of a vein from post-contrast images and then calculate only the susceptibility of venous blood based on the magnetic moment measured from pre-contrast images. This assumes that the size of the vein does not change before and after the injection of the contrast agent.

4.1.3. Orientation dependence—When the orientation of a cylindrical object deviates from 90° , but other factors remain the same, the magnetic moment quantified from the object becomes smaller than that at 90° (see Section 2.1). As a result, the uncertainty of the magnetic moment increases and so does that of the susceptibility. Eq. (A.1) reflects on the above statement. In order to reduce the uncertainty, one possibility is to increase the echo time and therefore the magnetic moment will become larger. When the orientation of the object is close to 0° , the uncertainty of the estimated susceptibility can be very large (see Eq. (A.2)). This is why for the parallel orientation, a two-echo approach will be better. Eq. (A.1) also indicates that the uncertainty of susceptibility approaches infinity when the orientation is close to the magic angle. For all quantified susceptibility values, each complex signal from the innermost radius, R_3 , is used in Eq. (7). As a result, the variables, $\delta Re(S_3)$, $\delta Im(S_3)$, and $\delta(S_i - S_j)$ for any i and j , are uncorrelated. The uncertainty of the susceptibility, Eq. (A.1), is derived based on this condition. For any choice of a radius larger than R_3 used in Eq. (7), some variables will become correlated and uncertainty formulas need to be rederived.

For the uncertainty of orientation, $\delta\theta$, low resolution images lead to a larger uncertainty than that quantified from high resolution images. For example, when we convert our phantom images to 4 mm isotropic resolution, on which our straw occupies only a few pixels, the error of the orientation can be up to $\pm 15^\circ$.

4.1.4. Techniques for background field removal—For phantom images, we have tried the high pass filter, quadratic fitting, and sophisticated harmonic artifact reduction for phase data (SHARP) [32] for removing background fields. The quadratic fitting technique is more reliable than the other two techniques when it is applied to our phantom images. High pass filter can remove the background field cleanly at the 90° and 75.5° cases, but not completely remove the background fields at the 28.2° orientation because of the geometry of the phantom container. SHARP, with a kernel size of 6, also shows a similar problem. In addition, after the application of SHARP, the phase values around the straw in the phantom are higher than expected, and the averaged phase value in the background is about 0.1 rad, larger than the noise level in phase images. Furthermore, when we apply SHARP and then our method, SWIM, and MEDI to the phantom images with the reduced matrix size of 128×128 , the quantified susceptibility values of our gadolinium straw become about 0.70 ppm, 0.48 ppm, and 0.55 ppm, respectively.

For human images, given the problems of SHARP described above and the uneasy application of the quadratic fitting technique, we chose to use the high pass filter for removing the background fields. The background phase around the vein was between 0.01 and 0.03 rad after the high pass filter was applied to the *in-vivo* data.

4.2. The unique solution from Eq. (7)

As Eq. (7) is a nonlinear function of the magnetic susceptibility, multiple solutions could exist. The number of possible solutions is discussed in the following two subsections. We overlap the range of g' in this section such that some freedom of choices will be allowed. More detailed mathematical descriptions are given in Appendix C.

4.2.1. $|g'| > 1.4$ leads to unique solution in one period—When the upper limit $|g'|$ of the integral in Eq. (7) is larger than 1.4, with a lower limit, $|\rho|/R^2 \geq 0.5$, the upper limit $|g'|$ can be replaced by infinity and the difference between the actual integral and the approximation is less than 5%. This condition can be achieved by choosing a sufficiently large R . As a result, φ_{in} in Eq. (7) can be uniquely determined between $2n\pi$ and $2(n+1)\pi$ with n being an arbitrary integer (see Eq. (C.2) in Appendix C.1). If we choose $B_0 = 3$ T and $T_E = 20$ ms, the possible solutions of χ between each adjacent 2π period will differ by at least 1 ppm. This means that susceptibilities of most biological tissues can be uniquely determined with just one echo time.

4.2.2. $0 < |g'| \leq 2$ leads to multiple solutions—Here we summarize our findings, as the detail descriptions and derivations are given in Appendix C.2. When $|g'|$ is in this range, we need to examine the number of roots in Eqs. (C.3) and (C.4). As the signs of $\beta \equiv (1 - 3 \cos \theta^2)/3$ and $Im(S)$ are known from measurements, the sign of $\beta Im(S)$ is known even before we solve Eq. (C.3). Based on derivations described in Appendix C.2, when the object orientation is larger than 24° , at most two roots can be solved from Eq. (C.3). However, if the orientation is less than 24° , then multiple solutions exist. Thus, in this scenario which includes the parallel orientation, we suggest solving the susceptibility with the two-echo approach.

4.2.3. Unknown materials with large susceptibility—For unknown materials with susceptibility values more than 4 ppm, an echo time shorter than 5 ms at 3 T will be needed in order to uniquely determine the susceptibility. However, this may be difficult to achieve and thus multiple echoes may be needed as described below.

As any solution in the form of $\varphi_{in} - 2n\pi$ satisfies Eq. (C.1), the actual solution of Eq. (7) may be determined from multiple echo gradient echo images. At least, the number of possible solutions will be reduced. For example, consider that phase $q_1 \equiv \varphi_{in,1} - 2n_1\pi$ is solved from echo time $T_{E,1}$ and $q_2 \equiv \varphi_{in,2} - 2n_2\pi$ is solved from echo time $T_{E,2}$. As $\varphi_{in,1}$ and $\varphi_{in,2}$ are proportional to $T_{E,1}$ and $T_{E,2}$, respectively, q_1 and q_2 satisfy the following equation

$$\frac{q_1 T_{E,2} - q_2 T_{E,1}}{\pi} = 2(n_2 T_{E,1} - n_1 T_{E,2}) \quad (15)$$

Obviously the left hand side of Eq. (15) is normally a real number but the right hand side demands that the equation has to be equal to an even integer, if the two echo times are chosen as integers in units of millisecond or sub-millisecond. This is only possible if Eq. (15) is zero. Hence, Eq. (15) limits possible values of n_1 and n_2 . As the magnetic moment ρ and $Im(S)$ are first measured, the subsequently solved susceptibility values $|\chi|$ will increase as $|n_i|$ increases. The solved object radius a will decrease but the solved spin density inside the object, $\rho_{0,c}$, will increase. However, since rough values of a and $\rho_{0,c}$ can be estimated from the magnitude image, ranges of n_1 and n_2 are limited and χ is likely to be uniquely determined with only two echo times. Choosing prime numbers for $T_{E,1}$ and $T_{E,2}$ in millisecond or sub-millisecond units (such as 5.9 ms or 10.9 ms) or using more echoes can very effectively reduce the possible solutions of χ . This is the main reason why at least a

double echo or a triple echo gradient echo sequence is preferred. However, the presence of thermal noise and systematic error may introduce more pseudo solutions.

4.3. Measurements and uncertainties from orientations close to 0°

For objects with orientations close to 0°, we may first estimate the value of a^2 from magnitude images. From Eq. (12), we can solve an initial value of χ . Then the updated radius of the object, a , can be calculated from either Eq. (10) or Eq. (11). The susceptibility value χ can be re-solved again from Eq. (12). As an iterative procedure, we can repeat the process to reach convergent solutions for the radius of the object, a , and its magnetic susceptibility, χ .

The uncertainty of susceptibility given in Eq. (B.2) is affected by the SNR inside the object of interest. When the ratio between $SNR_{0,c,1}$ and $SNR_{0,c,2}$ acquired from two echo times becomes large, the uncertainty of susceptibility will reduce. Thus, the echo spacing between the two echo times is better to be large. This is how the echo time combinations in the phantom experiments were selected (see comments in Table 7). In the simulations, we purposely show that the susceptibility of the object can still be quantified from the echo time combination of 17 ms and 20 ms (see Table 6), but with a larger uncertainty. Both phase values inside the object acquired from two echo times should not be concurrently multiples of π for susceptibility quantification, as Eqs. (B.2) and (13) indicate infinite uncertainty in this scenario. However, the uncertainty of the susceptibility can still be reasonably small, when only either $\phi_{in,1}$ or $\phi_{in,2}$ is a multiple of π . Nonetheless, in this situation, the uncertainties of quantified cross-sectional area and spin density inside the object from that particular echo time will become very large (e.g., see Eq. (B.5) and results at $T_E = 20$ ms in Tables 6, 7, 8, and 9). This is because when a $\phi_{in,n}$ is close to multiples of π , the imaginary part of the signal is close to zero and it becomes impractical to quantify the cross-sectional area and the spin density inside the object.

4.4. The limitations of our method and future work

Although our method is derived from the model of an infinitely long cylinder, such a model is valid when the ratio of the height to the diameter of a finite cylinder is larger than 5 to 1 [23]. In addition, the infinitely long cylinder model is also acceptable when any section of a curved cylinder is less than 30° [33]. Thus, for the susceptibility quantification of venous blood, our method is feasible to most *in vivo* medullary and pial veins, with the acquisitions of isotropic 3D gradient echo data from two echo times. Nonetheless, even with a perfect background phase removal procedure, local background phase due to the presence of other neighboring tissues may exist. A large local background phase such as 0.8 rad may lead to an incorrect center of the object of interest and an incorrect susceptibility value. Thus, our equations for the *in vivo* applications will require local background field corrections after the removal of the global background phase. We are currently revising the equations and engaging these studies.

In our current procedures, for reliable susceptibility quantifications, we suggest to choose the innermost circle with a radius (R_3) of at least 0.5 pixel from the boundary of the object and the differences between any two of the three radii to be at least 1 pixel. This leads to a

total of at least 2.5 pixels away from the boundary of a given object. If two or more cylindrical objects or vessels are close to each other, but have at least 5 pixels between their boundaries, then our method is still applicable to the susceptibility quantification of each object. However the accuracy of quantified susceptibility may be a concern. Our method also cannot accurately quantify the susceptibilities of two long cylinders when their nearest boundaries are within 5 pixels, unless they are parallel to the main field. In addition, Section 4.1.2 points out low SNR of an object such as a vein at a long echo time will increase the uncertainty (see Eqs. (A.1) and (7)). Thus, the steps of quantifying susceptibility and reducing uncertainty in the low SNR object are more complex. Currently we are investigating this situation. In addition, the uncertainty of quantified susceptibility values at the low orientation is large due to small g' . The two echo approach for the low orientation may reduce the uncertainty. We are also investigating this possibility to reduce the uncertainty of the quantified susceptibility.

5. Conclusion

Using a standard gradient echo sequence with one or two echo times, our method can accurately quantify magnetic moment, susceptibility, radius, and spin density ρ_0 and $\rho_{0,c}$ of a given cylindrical object at most orientations. The accuracy of quantified susceptibility can be improved by the orientation close to 90° , high SNR of the object, or a long echo time within the clinical range. Our approach has overcome two problems in estimating susceptibility: phase aliasing and partial volume effects. We have demonstrated the feasibility of this method through simulations, phantom, and *in-vivo* human studies. Our method provides an alternate approach for accurate susceptibility and radius quantifications of narrow cylinders.

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Appendix A. Uncertainty of susceptibility at a generic orientation: magnetic moment and susceptibility are quantified from the same image

In the evaluations of the following equations in this Appendix, positive magnetic moment value $|M|$ and positive susceptibility $|\chi|$ should be used.

When the susceptibility is quantified from S_3 , which is enclosed by a radius R_3 , the uncertainty of the susceptibility is given by

$$\frac{\delta \Delta x}{\Delta x} = \frac{\sqrt{\delta \theta^2 A^2 + \left(\frac{\delta Re(S_3)}{\pi \ell \sigma}\right)^2 B^2 + \left(\frac{\delta Im(S_3)}{\pi \ell \sigma}\right)^2 C^2 + \left(\frac{\delta(S_1 - S_2)}{\pi \ell \sigma}\right)^2 D^2 + \left(\frac{\delta(S_2 - S_3)}{\pi \ell \sigma}\right)^2 E^2}}{|\varphi/\sin\theta^2| |\text{SNR}_{0,c} (1 - 3\cos^2\theta)/3 - \text{SNR}_0 \sin\phi_{in} J_0(g')/g|} \quad (\text{A.1})$$

where $\text{SNR}_0 \equiv \rho_0/\sigma$ and $\text{SNR}_{0,c} \equiv \rho_{0,c}/\sigma$

$$\begin{aligned}
A &= 2|\varphi| \frac{\cos\theta}{\sin\theta} \left(\text{SNR}_0 \sin\phi_{in} \frac{J_0(g')}{g'} - \text{SNR}_{0,c} \right) \\
B &= -\sin\phi_{in} \\
C &= \cos\phi_{in} \\
D &= \sin\phi_{in} \left(\frac{h_3}{h_{12}} + \frac{h_{23} \left(\frac{h_3}{h_{12}} \left(\frac{J_0(\phi_2)}{\phi_2} - \frac{J_0(\phi_1)}{\phi_1} \right) + \frac{J_0(\phi_3)}{\phi_3} \right)}{h_{12} \frac{J_0(\phi_3)}{\phi_3} + h_{23} \frac{J_0(\phi_1)}{\phi_1} + h_{31} \frac{J_0(\phi_2)}{\phi_2}} \right) \\
E &= -\sin\phi_{in} \frac{\left(h_3 \left(\frac{J_0(\phi_2)}{\phi_2} - \frac{J_0(\phi_1)}{\phi_1} \right) + h_{12} \frac{J_0(\phi_3)}{\phi_3} \right)}{h_{12} \frac{J_0(\phi_3)}{\phi_3} + h_{23} \frac{J_0(\phi_1)}{\phi_1} + h_{31} \frac{J_0(\phi_2)}{\phi_2}}
\end{aligned} \quad (\text{A.2})$$

where $h_3 = \int_{\phi_3}^{|g'|} \frac{dx}{x^2} J_0(x)$, and $\phi_i \equiv |\varphi|/R_i^2$, $i=1, 2$ or 3

$$\begin{aligned}
h_{ij} &= \int_{\phi_i}^{\phi_j} \frac{dx}{x^2} J_0(x) \\
\frac{\delta Re(S_3)}{\pi \ell \sigma} &= \sqrt{\frac{\Delta x \Delta y R_3^2}{\pi} + \epsilon_R^2 \left(\varphi h_3 \text{SNR}_0 + \text{SNR}_{0,c} \cos\phi_{in} \frac{\varphi}{|g'|} \right)^2}
\end{aligned}$$

where ϵ_R is defined as the percentage change between the theoretical value of $Re(S_3)$ and summed $Re(S_3)$ directly from images.

$$\frac{\delta Im(S_3)}{\pi \ell \sigma} = \sqrt{\frac{\Delta x \Delta y R_3^2}{\pi} + \epsilon_I^2 \left(\text{SNR}_{0,c} \sin\phi_{in} \frac{\varphi}{|g'|} \right)^2}$$

where ϵ_I is defined as the percentage change between the theoretical value of $Im(S_3)$ and summed $Im(S_3)$ directly from images.

$$\frac{\delta(S_i - S_j)}{\pi \ell \sigma} = \sqrt{\frac{\Delta x \Delta y}{\pi} |R_i^2 - R_j^2| + \epsilon_{ij}^2 (\varphi h_{ij} \text{SNR}_0)^2}$$

where $\epsilon_{ij} \equiv \delta(S_i - S_j)/(S_i - S_j)$ for $i, j = 1, 2, 3$ and the index i or j refers to the circle within which the complex signal is added. Similarly, ϵ_{ij} should be interpreted as the percentage change between the theoretical $S_i - S_j$ (which is a real number) and the real part of summed $S_i - S_j$ directly from images.

The uncertainty of the spin density outside the object is calculated from $S_1 - S_2$ and is given by

$$\frac{\delta \rho_0}{\rho_0} = \frac{1}{\text{SNR}_0} \sqrt{\left(\frac{F}{\varphi} \right)^2 \left(\frac{\delta(S_1 - S_2)}{\pi \ell \sigma} \right)^2 + \left(\frac{G}{\varphi} \right)^2 \left(\frac{\delta(S_3 - S_2)}{\pi \ell \sigma} \right)^2}$$

where

$$\frac{F}{\wp} = \frac{1}{\wp h_{12}} + \frac{\frac{h_{23}}{h_{12}} \left(h_{12} + \frac{J_0(\phi_2)}{\phi_2} - \frac{J_0(\phi_1)}{\phi_1} \right)}{\wp \left(h_{12} \frac{J_0(\phi_3)}{\phi_3} + h_{23} \frac{J_0(\phi_1)}{\phi_1} + h_{31} \frac{J_0(\phi_2)}{\phi_2} \right)}$$

$$\frac{G}{\wp} = \frac{- \left(h_{12} + \frac{J_0(\phi_2)}{\phi_2} - \frac{J_0(\phi_1)}{\phi_1} \right)}{\wp \left(h_{12} \frac{J_0(\phi_3)}{\phi_3} + h_{23} \frac{J_0(\phi_1)}{\phi_1} + h_{31} \frac{J_0(\phi_2)}{\phi_2} \right)}$$

The cross-sectional area of a cylindrical object is defined as $A_0 \equiv \pi a^2$. Its uncertainty is given by

$$\frac{\delta A_0}{A_0} = \left[\left(\frac{A}{H} + 2 \cot \theta \right)^2 \delta \theta^2 + \left(\frac{B}{H} \right)^2 \left(\frac{\delta \text{Re}(S_3)}{\pi \ell \sigma} \right)^2 + \left(\frac{C}{H} \right)^2 \left(\frac{\delta \text{Im}(S_3)}{\pi \ell \sigma} \right)^2 \right. \\ \left. + \left(\frac{h_{23}}{I} + \frac{D}{H} \right)^2 \left(\frac{\delta(S_1 - S_2)}{\pi \ell \sigma} \right)^2 + \left(\frac{h_{12}}{I} - \frac{E}{H} \right)^2 \left(\frac{\delta(S_2 - S_3)}{\pi \ell \sigma} \right)^2 \right]^{1/2}$$

where

$$H = |\wp / \sin \theta^2| (\text{SNR}_{0,c} (1 - 3 \cos^2 \theta) / 3 - \text{SNR}_0 \sin \phi_{in} J_0(g') / g)$$

$$I = \wp \text{SNR}_0 \left(h_{12} \frac{J_0(\phi_3)}{\phi_3} + h_{23} \frac{J_0(\phi_1)}{\phi_1} + h_{31} \frac{J_0(\phi_2)}{\phi_2} \right)$$

The spin density inside the object is given by

$$\frac{\delta \rho_{0,c}}{\rho_{0,c}} = \left[\left(\frac{\delta \text{Im}(S_3)}{\pi \ell \sigma} \right)^2 \left(\frac{1}{a^2 \sin \phi_{in} \text{SNR}_{0,c}} + \frac{C}{H} (1 - \phi_{in} \cot \phi_{in}) \right)^2 \right. \\ \left. + \left(\frac{\delta \text{Re}(S_3)}{\pi \ell \sigma} \right)^2 \left(\frac{B}{H} (1 - \phi_{in} \cot \phi_{in}) \right)^2 \right. \\ \left. + \left(\frac{\delta(S_1 - S_2)}{\pi \ell \sigma} \right)^2 J^2 + \left(\frac{\delta(S_2 - S_3)}{\pi \ell \sigma} \right)^2 K^2 \right. \\ \left. + (\delta \theta)^2 \left(\frac{A}{H} (1 - \phi_{in} \cot \phi_{in}) - g \sin 2\theta \cot \phi_{in} + 2 \cot \theta \right)^2 \right]^{1/2}$$

where

$$J = \frac{D}{H} (1 - \phi_{in} \cot \phi_{in}) + \frac{h_{23}}{I}$$

$$K = \frac{E}{H} (1 - \phi_{in} \cot \phi_{in}) - \frac{h_{12}}{I}$$

Appendix B. Uncertainty of susceptibility for the parallel orientation

In this Appendix, subscripts 1 and 2 in the following equations refer to the values quantified from echo time T_{E1} and T_{E2} , respectively. They should not be confused with different radii used in the main text and the previous Appendix.

The uncertainty of the susceptibility is given by

$$\frac{\delta\Delta_X}{\Delta_X} = \left[\delta\theta^2 \left(- \right)^2 + \left(- \right)^2 \left(\frac{\delta\rho_{0,1}}{\rho_{0,1}} \right)^2 + \left(- \right)^2 \left(\frac{\delta\rho_{0,2}}{\rho_{0,2}} \right)^2 + \left(- \right)^2 \left(\frac{\delta Re(S_1)}{\ell\rho_{0,1}} \right)^2 + \left(- \right)^2 \left(\frac{\delta Re(S_2)}{\ell\rho_{0,2}} \right)^2 + \left(- \right)^2 \left(\frac{\delta Im(S_1)}{\ell\rho_{0,1}} \right)^2 + \left(- \right)^2 \left(\frac{\delta Im(S_2)}{\ell\rho_{0,2}} \right)^2 \right]^{1/2} \quad (B.1)$$

$$\begin{aligned} \mathbb{A} &= -\mathbb{I}\sin 2\theta \\ \mathbb{B} &= \tan\phi_{in,1} \left(\frac{Im(S_2)}{\ell\rho_{0,2}} - \frac{Re(S_2)}{\ell\rho_{0,2}} \tan\phi_{in,2} \right) \\ \mathbb{C} &= \tan\phi_{in,2} \left(\frac{Re(S_1)}{\ell\rho_{0,1}} \tan\phi_{in,1} - \frac{Im(S_1)}{\ell\rho_{0,1}} \right) \\ \mathbb{D} &= \tan\phi_{in,1} \tan\phi_{in,2} \\ \mathbb{E} &= -\mathbb{D} \\ \mathbb{F} &= -\tan\phi_{in,2} \\ \mathbb{G} &= \tan\phi_{in,1} \\ \mathbb{H} &= \frac{1}{3} (1 - 3\cos^2\theta) \mathbb{I} \\ \mathbb{I} &= \left(\frac{Re(S_1)}{\ell\rho_{0,1}} - \frac{Re(S_2)}{\ell\rho_{0,2}} \right) (g_1 \cdot \tan\phi_{in,2} + g_2 \cdot \tan\phi_{in,1}) \\ &+ \frac{Im(S_1)}{\ell\rho_{0,1}} (g_1 \tan\phi_{in,1} \tan\phi_{in,2} - g_2) - \frac{Im(S_2)}{\ell\rho_{0,2}} (g_2 \tan\phi_{in,1} \tan\phi_{in,2} - g_1) \end{aligned}$$

$$\frac{\delta Re(S_n)}{\ell\rho_{0,n}} = \sqrt{\Delta x \Delta y \frac{\pi R^2}{\text{SNR}_{0,n}^2} + \epsilon_R^2 \left(\frac{Re(S_n)}{\ell\rho_{0,n}} \right)^2} \quad (B.2)$$

$$\begin{aligned} \frac{\delta Im(S_n)}{\ell\rho_{0,n}} &= \sqrt{\Delta x \Delta y \frac{\pi R^2}{\text{SNR}_{0,n}^2} + \epsilon_I^2 \left(\frac{Im(S_n)}{\ell\rho_{0,n}} \right)^2} \\ \frac{\delta\rho_{0,n}}{\rho_{0,n}} &= \sqrt{\frac{\Delta x \Delta y}{\pi(R_a^2 - R_b^2) \text{SNR}_{0,n}^2} + \epsilon_{ab}^2} \end{aligned} \quad (B.3)$$

where ϵ_{ab} is the percentage error between the theoretical spin density and the measured spin density within the annular ring defined by radii R_a and R_b .

The uncertainty of the cross-sectional area quantified from each echo time is given by

$$\begin{aligned} \left(\frac{\delta A_0}{A_0} \right)_{T_{E1}} &= \left[\left(\frac{\delta Im(S_1)}{\ell\rho_{0,1}} \right)^2 \left(- + \frac{\cot\phi_{in,1}}{\ell\rho_{0,1}} \right)^2 + \left(\frac{\delta Im(S_2)}{\ell\rho_{0,2}} \right)^2 \left(- \right)^2 + \left(\frac{\delta Re(S_1)}{\ell\rho_{0,1}} \right)^2 \left(- - \frac{1}{\ell\rho_{0,1}} \right)^2 + \left(\frac{\delta Re(S_2)}{\ell\rho_{0,2}} \right)^2 \left(- \right)^2 + \left(\frac{\delta\rho_{0,1}}{\rho_{0,1}} \right)^2 \left(- + - \right)^2 + \left(\frac{\delta\rho_{0,2}}{\rho_{0,2}} \right)^2 \left(- \right)^2 + \delta\theta^2 \left(- + - \right)^2 \right]^{1/2} \quad (B.4) \end{aligned}$$

and

$$\begin{aligned} \left(\frac{\delta A_0}{A_0} \right)_{T_{E2}} &= \left[\left(\frac{\delta Im(S_1)}{\ell\rho_{0,1}} \right)^2 \left(- \right)^2 + \left(\frac{\delta Im(S_2)}{\ell\rho_{0,2}} \right)^2 \left(- + \frac{\cot\phi_{in,1}}{\ell\rho_{0,1}} \right)^2 + \left(\frac{\delta Re(S_1)}{\ell\rho_{0,1}} \right)^2 \left(- \right)^2 + \left(\frac{\delta Re(S_2)}{\ell\rho_{0,2}} \right)^2 \left(- - \frac{1}{\ell\rho_{0,2}} \right)^2 + \left(\frac{\delta\rho_{0,1}}{\rho_{0,1}} \right)^2 \left(- \right)^2 + \left(\frac{\delta\rho_{0,2}}{\rho_{0,2}} \right)^2 \left(- + - \right)^2 + \delta\theta^2 \left(- + - \right)^2 \right]^{1/2} \quad (B.5) \end{aligned}$$

where the subscript n used in the following definitions refers to each variable obtained at the n^{th} echo time T_{En} , as those variables depend on the echo time.

$$\begin{aligned}\mathbb{J} &= A_0 \left(1 + \frac{g_n'^2}{4} - \frac{g_n'^2 a^2}{2R^2} \right) \\ \mathbb{K} &= -\phi_{in,n} \frac{Im(S_n)}{\ell_{\rho_{0,n}}} \csc^2 \phi_{in,n} - \pi (R^2 - a^2) \frac{g_n'^2 a^2}{2R^2} \\ \mathbb{L} &= -g_n \frac{Im(S_n)}{\ell_{\rho_{0,n}}} \csc^2 \phi_{in,n} \sin 2\theta - \pi (R^2 - a^2) \frac{g_n'^2 a^2}{R^2} \cot \theta \\ \mathbb{M} &= \pi (R^2 - a^2) \left(1 - \frac{g_n'^2 a^2}{4R^2} \right)\end{aligned}$$

If the cross-sectional area is averaged from two echo times, its uncertainty is given by

$$\begin{aligned}\frac{\delta A_0}{A_0} &= N^{-1} \left[\left(\frac{\delta Re(S_1)}{\ell_{\rho_{0,1}}} \right)^2 (1 + \mathbb{O})^2 + \left(\frac{\delta Re(S_2)}{\ell_{\rho_{0,2}}} \right)^2 (1 + \mathbb{O})^2 \right. \\ &+ \left(\frac{\delta Im(S_2)}{\ell_{\rho_{0,2}}} \right)^2 (\cot \phi_{in,2} - \mathbb{O})^2 + \left(\frac{\delta Im(S_1)}{\ell_{\rho_{0,1}}} \right)^2 (\cot \phi_{in,1} - \mathbb{O})^2 \\ &+ \left(\frac{\delta \rho_{0,1}}{\rho_{0,1}} \right)^2 (\mathbb{C} \cot \phi_{in,1} \cot \phi_{in,2} - \mathbb{O})^2 \\ &\left. + \left(\frac{\delta \rho_{0,2}}{\rho_{0,2}} \right)^2 (\mathbb{B} \cot \phi_{in,1} \cot \phi_{in,2} - \mathbb{O})^2 + (\delta \theta)^2 \mathbb{P}^2 \right]^{1/2} \quad (\text{B.6})\end{aligned}$$

where

$$\begin{aligned}N &= 2A_0 \left(1 + \frac{g_1'^2 + g_2'^2}{8} - \frac{(g_1'^2 + g_2'^2) a^2}{4R^2} \right) \\ \mathbb{O} &= \frac{Im(S_1)}{\ell_{\rho_{0,1}}} \phi_{in,1} \csc^2 \phi_{in,1} + \frac{Im(S_2)}{\ell_{\rho_{0,2}}} \phi_{in,2} \csc^2 \phi_{in,2} + \pi (R^2 - a^2) \frac{(g_1'^2 + g_2'^2) a^2}{2R^2} \\ \mathbb{P} &= \pi (R^2 - a^2) \frac{a^2}{R^2} \left(\frac{2}{1 - 3\cos^2 \theta} \right) (g_1^2 + g_2^2) \sin^3 \theta \cos \theta\end{aligned}$$

The uncertainty of the spin density inside the object quantified from each echo time is given by

$$\begin{aligned}\frac{\delta \rho_{0,c,1}}{\rho_{0,c,1}} &= \left[\left(\frac{\delta \rho_{0,1}}{\rho_{0,1}} \right)^2 (- + - \mathbb{Q})^2 + \left(\frac{\delta \rho_{0,2}}{\rho_{0,2}} \right)^2 (-\mathbb{Q})^2 + \left(\frac{\delta Re(S_1)}{\ell_{\rho_{0,1}}} \right)^2 (1 - -\mathbb{Q})^2 \right. \\ &+ \left(\frac{\delta Re(S_2)}{\ell_{\rho_{0,2}}} \right)^2 (-\mathbb{Q})^2 + \left(\frac{\delta Im(S_1)}{\ell_{\rho_{0,1}}} \right)^2 \left(\frac{\ell_{\rho_{0,1}}}{Im(S_1)} - -\mathbb{Q} - \frac{\cot \phi_{in,1}}{Im(S_1)} \right)^2 \\ &\left. + \left(\frac{\delta Im(S_2)}{\ell_{\rho_{0,2}}} \right)^2 (-\mathbb{Q})^2 + \delta \theta^2 (-\mathbb{Q} + - + g_1 \cot \phi_{in,1} \sin 2\theta)^2 \right]^{1/2} \\ \frac{\delta \rho_{0,c,2}}{\rho_{0,c,2}} &= \left[\left(\frac{\delta \rho_{0,1}}{\rho_{0,1}} \right)^2 (-\mathbb{Q})^2 + \left(\frac{\delta \rho_{0,2}}{\rho_{0,2}} \right)^2 (- + - \mathbb{Q})^2 + \left(\frac{\delta Re(S_1)}{\ell_{\rho_{0,1}}} \right)^2 (-\mathbb{Q})^2 \right. \\ &+ \left(\frac{\delta Re(S_2)}{\ell_{\rho_{0,2}}} \right)^2 (1 - -\mathbb{Q})^2 + \left(\frac{\delta Im(S_1)}{\ell_{\rho_{0,1}}} \right)^2 (-\mathbb{Q})^2 \\ &\left. + \left(\frac{\delta Im(S_2)}{\ell_{\rho_{0,2}}} \right)^2 \left(\frac{\ell_{\rho_{0,2}}}{Im(S_2)} - -\mathbb{Q} - \frac{\cot \phi_{in,2}}{Im(S_2)} \right)^2 + \delta \theta^2 (-\mathbb{Q} + - + g_2 \cot \phi_{in,2} \sin 2\theta)^2 \right]^{1/2} \\ \mathbb{Q} &= - + \phi_{in,n} \cot \phi_{in,n}\end{aligned}$$

where the subscript n again refers to each variable measured at the n^{th} echo time T_{En} .

If we use Eq. (B.6) to further estimate the uncertainty of spin density inside the object at each echo time, these two uncertainties are given by

$$\begin{aligned} \frac{\delta\rho_{0,c,n}}{\rho_{0,c,n}} = & \left[\delta\theta^2 \mathbb{R}^2 + \left(\frac{\delta\rho_{0,1}}{\rho_{0,1}} \right)^2 \left(-\mathbb{S} - \mathbb{T} \right)^2 + \left(\frac{\delta\rho_{0,2}}{\rho_{0,2}} \right)^2 \left(-\mathbb{S} + \mathbb{T} \right)^2 \right. \\ & + \left(\frac{\delta Re(S_1)}{\ell\rho_{0,1}} \right)^2 \left(\frac{1}{2} + \mathbb{S} \right)^2 + \left(\frac{\delta Re(S_2)}{\ell\rho_{0,2}} \right)^2 \left(\frac{1}{2} - \mathbb{S} \right)^2 \\ & + \left(\frac{\delta Im(S_1)}{\ell\rho_{0,1}} \right)^2 \left(-\mathbb{S} + \delta_{n,1} \frac{\ell\rho_{0,1}}{Im(S_1)} - \frac{\cot\phi_{in,1}}{2} \right)^2 \\ & \left. + \left(\frac{\delta Im(S_2)}{\ell\rho_{0,2}} \right)^2 \left(-\mathbb{S} + \delta_{n,2} \frac{\ell\rho_{0,2}}{Im(S_2)} - \frac{\cot\phi_{in,2}}{2} \right)^2 \right]^{1/2} \end{aligned}$$

where $\delta_{n,1}$ and $\delta_{n,2}$ are Kronecker delta functions. Again, the subscript n refers to each variable measured at the n^{th} echo time T_{E_n} .

$$\begin{aligned} \mathbb{R} &= \frac{\mathbb{P}}{2} + \cot\phi_{in,n} \left(-\phi_{in,n} + g_n \sin 2\theta \right) \\ \mathbb{S} &= -\phi_{in,n} \cot\phi_{in,n} \\ \mathbb{T} &= \cot\phi_{in,1} \cot\phi_{in,2} \end{aligned}$$

Appendix C. The unique solution of Eq. (7)

In this section, g' will be separated into two regimes, $g' > 1.4$ and $0 < g' < 2$. As $J_0(x)/x^2$ is an even function, Eq. (7) is invariant even if the sign of magnetic susceptibility, χ , is changed. Thus, we only consider the positive magnetic susceptibility in the following discussions. This means that g , g' , and φ are also considered to be positive.

Appendix C.1. $g' > 1.4$

If φ/R^2 is no more than 0.5 radian, g' can be replaced by infinity in Eq. (7). This replacement leads to less than 5% deviation from the original result of the integral. Eq. (7) can be rewritten and easily solved.

$$Re(S) \sin\phi_{in} = Im(S) \cos\phi_{in} + \pi\ell\rho_0\varphi \sin\phi_{in} \int_{\varphi/R^2}^{\infty} dx J_0(x) / x^2 \quad (C.1)$$

$$\phi_{in} = \tan^{-1} \frac{Im(S)}{Re(S) - \pi\ell\rho_0\varphi \int_{\varphi/R^2}^{\infty} dx \frac{J_0(x)}{x^2}} + 2n\pi \quad (C.2)$$

where n is any integer. Note that it is $2n\pi$ rather than $n\pi$ in the above solution, as the sign of $Im(S)$ is known in Eq. (C.1).

Appendix C.2. $0 < g' < 2$

The phase inside the object φ_{in} can be rewritten as $\beta g = \beta g'/a$, with $a \equiv \sin \vartheta$ and $\beta = (1 - 3 \cos \vartheta)/3$. Therefore, Eq. (7) can be rewritten as the following

$$f(g') \equiv Im(S) \cot\left(\frac{\beta}{a} g'\right) + \pi\ell\rho_0\varphi \int_{\varphi/R^2}^{g'} \frac{J_0(x)}{x^2} dx - Re(S) \quad (C.3)$$

The first derivative of $f(g')$ is

$$\begin{aligned}
f'(g') &= -\frac{\beta}{\alpha} \text{Im}(S) \cdot \csc^2\left(\frac{\beta}{\alpha} g'\right) + \pi \ell \rho_0 \wp \frac{J_0(g')}{g'^2} \\
&= \csc^2\left(\frac{\beta}{\alpha} g'\right) \left[-\frac{\beta}{\alpha} \text{Im}(S) + \left(\frac{\beta}{\alpha}\right)^2 \pi \ell \rho_0 \wp J_0(g') \text{sinc}^2 \phi_{in} \right] \quad (\text{C.4}) \\
&= \csc^2\left(\frac{\beta}{\alpha} g'\right) \left[-\frac{\beta}{\alpha} \text{Im}(S) + k(\phi_{in}) \right]
\end{aligned}$$

$$\text{where } k(\phi_{in}) \equiv \left(\frac{\beta}{\alpha}\right)^2 \pi \ell \rho_0 \wp J_0(g') \text{sinc}^2 \phi_{in}.$$

Clearly, if $\beta \text{Im}(S) < 0$, then $f'(g')$ will always be positive and therefore, by the mean value theorem in calculus, only one root exists in $f(g') = 0$. As $\beta \text{Im}(S)$ is proportional to $\beta \sin(\phi_{in}) = \beta \sin(\beta g) = |\beta| \sin(|\beta g|) = |\beta| \sin(|\phi_{in}|)$, when $\beta \text{Im}(S) < 0$, this implies that $|\phi_{in}|$ is between $(2n-1)\pi$ and $2n\pi$, with n being any positive integer.

On the other hand, when $\beta \text{Im}(S) > 0$, this implies that $|\phi_{in}|$ is between $(2n-2)\pi$ and $(2n-1)\pi$. When $|\phi_{in}| < \pi$, Fig. 5 indicates at most one solution from $f'(g') = 0$. Again, by the mean value theorem, at most two solutions can exist in $f(g') = 0$.

When $\beta \text{Im}(S) > 0$ and $2n\pi < |\phi_{in}| < (2n+1)\pi$ with n being a positive integer, Fig. 5 or Eq. (C.4) indicates that up to two roots can be solved from $f'(g') = 0$ in each n range. This means that at most three solutions can exist in every π range of $f(g') = 0$. Given $0 < g' = ag < 2$ and $\phi_{in} \equiv \beta g$ in the current discussions, we can further derive that

$$0 < 1 - \cos^2 \theta = \alpha < \frac{2}{3(n\pi+1)} \quad (\text{C.5})$$

and

$$-\frac{2}{3} < \beta < -\frac{2n\pi}{3(n\pi+1)} \quad (\text{C.6})$$

When $n = 1$, α is less than 0.161, β is less than -0.506 , and the orientation of the object is less than 24° from the main field.

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Fig. 1.

(a) A cylinder has an orientation θ relative to the main field. (b) A schematic drawing shows the cross section of a cylindrical object with radius a , enclosed by three coaxial pseudo cylinders (or circles) whose radii are R_1 , R_2 , and R_3 . The MR signal within each pseudo cylinder (or circle) is S_1 , S_2 , and S_3 , respectively.

Fig. 2.

(a) The magnitude and (b) its associated filtered phase image at echo time 20 ms were acquired from a 3 T machine. The straw filled with a Gd-DPTA solution has a diameter of 4.92 ± 0.02 mm. The straw was immersed in the gel phantom and was perpendicular to the main field.

Fig. 3. (a) Magnitude and (b) its associated phase image of a volunteer acquired from a 3D gradient echo image at $T_E = 19.2$ ms of 4 T. The vein whose susceptibility is analyzed in this work is indicated by arrows.

Fig. 4.

(a) Coronal view of the same vein (indicated by a white arrow) as shown in Fig. 3. The direction of the main field is shown by the yellow arrow. The orientation of this vein is 80° relative to the main field. The same vein (inside circles) is also displayed in the (b) sagittal magnitude and (c) its associated phase image. (d) The enlarged magnitude image of (b). (e) The enlarged phase image of (c).

Fig. 5.

A plot of $k(\varphi_{in}) \equiv \pi \ell \rho_0 (\beta/\alpha)^2 \mathcal{P} \text{sinc}^2(\varphi_{in}) J_0(g')$ versus φ_{in} . The plot is generated with $\theta = 90^\circ$, $\alpha/\beta = 0.111$, $\mathcal{P} = 6.02$, $\rho_0 = 10.0$, $\ell = 1$, $g' = 1.5$, and $\text{Im}(S) = 1000$. $k(\varphi_{in})$ is defined in Eq. (C.4). This function is monotonically decreased between 0 and π and starts oscillating beyond π . The actual imaginary part of the signal is represented by a horizontal line. The intersection of the horizontal line and the curve indicates the solution of $f'(g')$.

Table 1

Quantified results from simulated images at three different echo times and three orientations.

Angle (degree)	T_E (ms)	ρ (rad-pixel ²)	χ ppm	A_0 pixel ²	$A_{0,c}$	A_0
90	11	2.21 ± 0.49 (2.21)	0.54 ± 0.18	2.90 ± 0.98	20.3 ± 4.3	9.86 ± 0.20
	17	3.42 ± 0.31 (3.41)	0.50 ± 0.06	3.14 ± 0.41	18.4 ± 2.0	9.83 ± 0.20
	20	4.01 ± 0.16 (4.01)	0.49 ± 0.04	3.14 ± 0.35	17.9 ± 1.8	9.84 ± 0.15
70	11	1.95 ± 0.51 (1.95)	0.57 ± 0.28	2.78 ± 1.39	20.9 ± 6.3	9.87 ± 0.20
	17	3.01 ± 0.45 (3.01)	0.52 ± 0.11	3.02 ± 0.63	19.0 ± 3.0	9.84 ± 0.20
	20	3.51 ± 0.28 (3.54)	0.52 ± 0.09	3.02 ± 0.57	18.4 ± 2.6	9.85 ± 0.20
40	11	0.70 ± 1.75 (0.91)	0.52 ± 1.56	2.32 ± 13.9	20.1 ± 124.6	9.77 ± 0.22
	17	1.55 ± 0.67 (1.41)	0.42 ± 0.34	4.08 ± 4.49	13.4 ± 13.4	9.90 ± 0.20
	20	1.82 ± 0.56 (1.66)	0.44 ± 0.25	3.94 ± 3.23	12.9 ± 9.5	9.91 ± 0.20

The actual values are: $\chi = 0.5$ ppm, $A_0 = 3.14$ pixel², $\rho_0 = 10$, and $\rho_{0,c}$ at different echo times are given in the text. The first column lists the orientation. The second column lists the echo time. The third column lists magnetic moment ρ calculated from the method in [21]. Numbers inside the parentheses are the theoretical ρ -values. The fourth column lists χ solved from Eq. (7). The chosen radius, R_3 , for solving χ is 1.5 pixel. The fifth column lists the cross-sectional area of the cylinder. The sixth column lists the effective spin density inside the object calculated from the imaginary part of Eq. (4). The seventh column lists the effective spin density outside the object calculated from Eq. (6).

Table 2

Quantified results from phantom images of the original image resolution at three different echo times and three orientations.

		Slice number 12					Slice number 16					
Angle (degree)	T_E (ms)	ρ (rad-mm ²)	ρ (rad-mm ²)	χ ppm	A_0 mm ²	$\rho_{0,z}/1000$	ρ_0	ρ (rad-mm ²)	χ ppm	A_0 mm ²	$\rho_{0,z}/1000$	ρ_0
90	11	15.4	14.1 $\pm$ 0.7	0.57 $\pm$ 0.02	17.6 $\pm$ 0.5	2.85 $\pm$ 0.06	1235 $\pm$ 12	14.5 $\pm$ 0.7	0.57 $\pm$ 0.02	18.2 $\pm$ 0.5	2.72 $\pm$ 0.05	1246 $\pm$ 12
	17	23.9	21.9 $\pm$ 0.5	0.54 $\pm$ 0.01	19.2 $\pm$ 0.4	2.49 $\pm$ 0.02	1218 $\pm$ 12	22.4 $\pm$ 0.4	0.55 $\pm$ 0.01	19.2 $\pm$ 0.2	2.55 $\pm$ 0.03	1224 $\pm$ 12
	20	28.2	26.3 $\pm$ 0.5	0.54 $\pm$ 0.01	19.0 $\pm$ 0.4	2.37 $\pm$ 0.05	1208 $\pm$ 12	26.2 $\pm$ 0.5	0.55 $\pm$ 0.01	18.7 $\pm$ 0.4	2.40 $\pm$ 0.05	1213 $\pm$ 12
75.5	11	14.5	12.9 $\pm$ 0.9	0.58 $\pm$ 0.04	16.9 $\pm$ 0.8	2.83 $\pm$ 0.10	1216 $\pm$ 12	13.0 $\pm$ 0.9	0.60 $\pm$ 0.04	16.5 $\pm$ 0.8	2.83 $\pm$ 0.11	1232 $\pm$ 12
	17	22.4	21.3 $\pm$ 0.4	0.54 $\pm$ 0.03	19.3 $\pm$ 0.6	2.49 $\pm$ 0.10	1203 $\pm$ 12	21.1 $\pm$ 0.4	0.56 $\pm$ 0.04	18.6 $\pm$ 0.6	2.53 $\pm$ 0.10	1213 $\pm$ 12
	20	26.4	24.6 $\pm$ 0.5	0.54 $\pm$ 0.03	19.0 $\pm$ 0.8	2.38 $\pm$ 0.10	1197 $\pm$ 12	24.5 $\pm$ 0.5	0.56 $\pm$ 0.03	18.2 $\pm$ 0.7	2.36 $\pm$ 0.09	1206 $\pm$ 12
28.2	11	3.45	3.64 $\pm$ 2.87	0.60 $\pm$ 0.27	19.3 $\pm$ 38.6	2.63 $\pm$ 5.06	1280 $\pm$ 13	3.22 $\pm$ 3.22	0.65 $\pm$ 0.53	15.8 $\pm$ 31.5	3.13 $\pm$ 7.20	1267 $\pm$ 13
	17	5.34	6.25 $\pm$ 3.75	0.55 $\pm$ 0.13	23.4 $\pm$ 21.5	2.16 $\pm$ 2.03	1280 $\pm$ 13	6.11 $\pm$ 3.85	0.57 $\pm$ 0.13	22.6 $\pm$ 20.3	2.36 $\pm$ 2.22	1274 $\pm$ 13
	20	6.29	6.65 $\pm$ 3.39	0.57 $\pm$ 0.10	20.4 $\pm$ 18.0	2.32 $\pm$ 2.23	1268 $\pm$ 13	6.97 $\pm$ 3.07	0.56 $\pm$ 0.10	21.9 $\pm$ 19.3	2.13 $\pm$ 2.04	1274 $\pm$ 13

Two different slices, 12 and 16, were analyzed. The theoretical value of χ is 0.58 ± 0.05 ppm and the actual cross-sectional area is 19.0 ± 0.2 mm². The SNR around and outside the straw for all three echo times is about 30:1. The SNR values inside the straw at three echo times, 11, 17, and 20 ms, are about 48:1, 44:1, and 42:1, respectively. The first column lists the orientation. The second column lists the echo time. The third column shows the theoretical ρ . The fourth and ninth column show quantified ρ . The fifth and tenth column list χ solved from Eq. (7). The sixth and eleventh columns show the cross-sectional area of the cylinder. The seventh and twelfth columns list the effective spin density inside the object calculated from the imaginary part of Eq. (4). The eighth and thirteenth columns list the effective spin density outside the object calculated from Eq. (6).

Table 3

Quantified results from phantom images of reduced 128×128 matrix size at three different echo times and three orientations.

		Slice number 12					Slice number 16					
Angle (degree)	T_E (ms)	ρ (rad $\cdot$ mm 2)	ρ (rad $\cdot$ mm 2)	χ ppm	A_0 mm 2	$\rho_{0c}/1000$	ρ_0	ρ (rad $\cdot$ mm 2)	χ ppm	A_0 mm 2	$\rho_{0c}/1000$	ρ_0
90	11	3.85	3.30 $\pm$ 0.46	0.55 $\pm$ 0.05	4.30 $\pm$ 0.43	11.1 $\pm$ 0.6	4911 $\pm$ 74	3.27 $\pm$ 0.46	0.57 $\pm$ 0.05	4.01 $\pm$ 0.40	11.7 $\pm$ 0.6	4948 $\pm$ 74
	17	5.98	5.46 $\pm$ 0.44	0.51 $\pm$ 0.04	4.91 $\pm$ 0.34	9.1 $\pm$ 0.4	4860 $\pm$ 97	5.69 $\pm$ 0.46	0.59 $\pm$ 0.04	4.45 $\pm$ 0.31	10.4 $\pm$ 0.4	4902 $\pm$ 98
	20	7.05	6.27 $\pm$ 0.44	0.54 $\pm$ 0.03	4.52 $\pm$ 0.27	9.1 $\pm$ 0.5	4825 $\pm$ 96	6.41 $\pm$ 0.44	0.54 $\pm$ 0.03	4.68 $\pm$ 0.28	8.9 $\pm$ 0.4	4842 $\pm$ 97
75.5	11	3.63	3.14 $\pm$ 0.94	0.55 $\pm$ 0.07	4.30 $\pm$ 0.69	10.3 $\pm$ 1.2	4880 $\pm$ 73	3.24 $\pm$ 0.97	0.60 $\pm$ 0.07	4.08 $\pm$ 0.65	11.0 $\pm$ 1.3	4864 $\pm$ 73
	17	5.60	4.92 $\pm$ 0.69	0.54 $\pm$ 0.04	4.45 $\pm$ 0.36	9.7 $\pm$ 0.6	4792 $\pm$ 96	4.94 $\pm$ 0.69	0.55 $\pm$ 0.04	4.45 $\pm$ 0.31	9.9 $\pm$ 0.6	4827 $\pm$ 97
	20	6.60	5.79 $\pm$ 0.46	0.53 $\pm$ 0.03	4.60 $\pm$ 0.18	9.0 $\pm$ 0.4	4773 $\pm$ 95	5.93 $\pm$ 0.47	0.55 $\pm$ 0.03	4.52 $\pm$ 0.18	9.5 $\pm$ 0.4	4809 $\pm$ 96
28.2	11	0.86	1.14 $\pm$ 0.97	0.46 $\pm$ 0.35	7.94 $\pm$ 16	7.1 $\pm$ 21	5136 $\pm$ 77	1.08 $\pm$ 0.92	0.52 $\pm$ 0.40	6.61 $\pm$ 13	8.0 $\pm$ 24	5084 $\pm$ 76
	17	1.34	1.28 $\pm$ 0.70	0.59 $\pm$ 0.37	4.45 $\pm$ 13	10.5 $\pm$ 37	5031 $\pm$ 101	1.52 $\pm$ 0.84	0.56 $\pm$ 0.35	5.56 $\pm$ 17	8.2 $\pm$ 29	4978 $\pm$ 100
	20	1.57	1.78 $\pm$ 0.80	0.55 $\pm$ 0.10	5.64 $\pm$ 7.33	7.7 $\pm$ 10	5002 $\pm$ 100	1.83 $\pm$ 0.82	0.56 $\pm$ 0.10	5.73 $\pm$ 7.44	7.6 $\pm$ 9.9	4936 $\pm$ 99

Two different slices, 12 and 16, were again analyzed. The theoretical value of χ is still 0.58 ± 0.05 ppm but the cross-sectional area becomes 4.75 ± 0.05 mm 2 . The SNR around and outside the straw for all three echo times is about 60:1. The SNR values inside the straw at three echo times, 11, 17, and 20 ms, are about 96:1, 88:1, and 84:1, respectively. The meaning of each column has been explained in Table 2.

Table 4

Quantified results from phantom images of the reduced 100×100 matrix size at three different echo times and three orientations.

		Slice number 12					Slice number 16					
Angle (degree)	T_E (ms)	ρ (rad $\cdot$ mm 2)	ρ (rad $\cdot$ mm 2)	χ ppm	A_0 mm 2	$\rho_{0,c}/1000$	ρ_0	ρ (rad $\cdot$ mm 2)	χ ppm	A_0 mm 2	$\rho_{0,c}/1000$	ρ_0
90	11	2.35	1.87 $\pm$ 0.54	0.50 $\pm$ 0.14	2.66 $\pm$ 0.82	17.2 $\pm$ 2.7	7953 $\pm$ 119	2.03 $\pm$ 0.51	0.57 $\pm$ 0.17	2.54 $\pm$ 0.79	19.1 $\pm$ 3.0	8034 $\pm$ 120
	17	3.64	3.62 $\pm$ 0.43	0.55 $\pm$ 0.05	3.02 $\pm$ 0.30	17.0 $\pm$ 1.2	7795 $\pm$ 156	3.52 $\pm$ 0.46	0.53 $\pm$ 0.05	3.08 $\pm$ 0.31	16.2 $\pm$ 1.1	7900 $\pm$ 157
	20	4.30	3.86 $\pm$ 0.54	0.55 $\pm$ 0.06	2.78 $\pm$ 0.28	16.0 $\pm$ 1.4	7943 $\pm$ 159	4.08 $\pm$ 0.49	0.54 $\pm$ 0.05	2.95 $\pm$ 0.30	15.2 $\pm$ 1.4	7947 $\pm$ 158
75.5	11	2.21	1.99 $\pm$ 0.98	0.54 $\pm$ 0.24	2.78 $\pm$ 1.42	18 $\pm$ 8	7921 $\pm$ 119	2.03 $\pm$ 0.99	0.61 $\pm$ 0.27	2.54 $\pm$ 1.30	20 $\pm$ 6	7921 $\pm$ 119
	17	3.42	3.31 $\pm$ 0.86	0.51 $\pm$ 0.12	3.20 $\pm$ 0.80	15.4 $\pm$ 1.8	7783 $\pm$ 156	3.20 $\pm$ 0.83	0.55 $\pm$ 0.13	2.83 $\pm$ 0.71	17.0 $\pm$ 2.0	7883 $\pm$ 158
	20	4.03	3.60 $\pm$ 0.86	0.54 $\pm$ 0.12	2.77 $\pm$ 0.67	15.8 $\pm$ 2.2	7757 $\pm$ 155	3.81 $\pm$ 0.91	0.55 $\pm$ 0.13	2.90 $\pm$ 0.69	15.4 $\pm$ 2.2	7828 $\pm$ 156
28.2	11	0.53	0.57 $\pm$ 1.14	0.57 $\pm$ 1.14	3.20 $\pm$ 19.2	16 $\pm$ 128	8279 $\pm$ 124	0.67 $\pm$ 1.34	0.58 $\pm$ 2.32	3.66 $\pm$ 22.0	14 $\pm$ 113	8275 $\pm$ 124
	17	0.81	0.87 $\pm$ 0.77	0.57 $\pm$ 0.39	3.14 $\pm$ 5.97	15 $\pm$ 23	8279 $\pm$ 166	0.94 $\pm$ 0.84	0.56 $\pm$ 0.39	3.46 $\pm$ 6.58	14 $\pm$ 21	8180 $\pm$ 164
	20	0.96	1.21 $\pm$ 0.39	0.53 $\pm$ 0.13	4.01 $\pm$ 4.41	11.2 $\pm$ 11.2	8270 $\pm$ 165	1.14 $\pm$ 0.36	0.55 $\pm$ 0.13	3.66 $\pm$ 4.03	12.5 $\pm$ 12.5	8156 $\pm$ 163

Two different slices, 12 and 16, were analyzed. The theoretical value of χ is still 0.58 ± 0.05 ppm but the cross-sectional area becomes 2.90 ± 0.03 mm 2 . The SNR outside the straw for all three echo times is about 77:1. The SNR values inside the straw at three echo times, 11, 17, and 20 ms, are about 123:1, 113:1, and 108:1, respectively. The meaning of each column has been explained in Table 2.

Table 5
Quantified magnetic susceptibilities of slice 16 at the 90° orientation from Tables 2 and 3, using SWIM and MEDI.

Angle (degree)	T_E (ms)	Our approach			SWIM ^a			MEDI ^b		
		256 × 256 ppm	128 × 128 ppm	256 × 256 ppm	128 × 128 ppm	256 × 256 ppm	128 × 128 ppm	256 × 256 ppm	128 × 128 ppm	256 × 256 ppm
90	11	0.57 ± 0.02	0.57 ± 0.05	0.36 ± 0.02	0.31 ± 0.04	0.42 ± 0.01	0.39 ± 0.06			
	17	0.55 ± 0.01	0.59 ± 0.04	0.36 ± 0.08	0.27 ± 0.07	0.40 ± 0.11	0.36 ± 0.06			
	20	0.55 ± 0.01	0.54 ± 0.03	0.35 ± 0.07	0.30 ± 0.12	0.40 ± 0.09	0.36 ± 0.16			

For comparisons, results from our method are listed again. The theoretical value of χ' is 0.58 ± 0.05 ppm. The first column lists the orientation. The second column lists the echo time. The third and fourth columns show quantified susceptibility values from our approach. The fifth and sixth columns show quantified susceptibility values from SWIM [11]. The seventh and eighth columns show quantified susceptibility values from MEDI [17]. The regularization parameters used in MEDI were suggested in their MATLAB code. Optimal choices of those regularization parameters are not known yet [34].

^aThresholding parameter = 0.1.

^bRegularization parameter = 250.

Table 6

Quantified results from simulated images using two different echo times when the object is parallel to the main field.

T_E (ms)	χ ppm	A_0 pixel ²	$\rho_{0,c}$	ρ_0
11	0.51 ± 0.03 (11/17)	2.90 ± 0.38	19.0 ± 2.7	9.90 ± 0.20
17		2.90 ± 1.33	18.5 ± 11.8	9.89 ± 0.20
20	0.51 ± 0.06 (20/17)	2.90 ± 3.76	14.4 ± 21.8	9.89 ± 0.20

The first column lists the echo time. The second column lists χ solved from Eq. (13). Numbers inside parentheses show the two echo times used for calculating the susceptibility. The theoretical value of χ is 0.5 ppm and the theoretical cross-sectional area is 3.14 pixel². The chosen radius, R , for solving Eq. (13) is 1.5 pixel. The third column lists the cross-sectional area of the cylinder calculated from Eq. (8). The fourth column lists the effective spin density inside the object calculated from the imaginary part used in Eq. (8). The fifth column lists the quantified effective spin density outside the object.

Table 7

Quantified results from phantom images of the original image resolution at two slices using two different echo times when the object is parallel to the main field.

T_E (ms)	Slice number 12			Slice number 16		
	χ ppm	A_0 mm ²	ρ_0	χ ppm	A_0 mm ²	ρ_0
11		21.7 ± 0.4	2424 ± 97	1355 ± 14	21.6 ± 0.4	2388 ± 96
17	0.56 ± 0.01 ^a	21.4 ± 3.2	2332 ± 560	1350 ± 14	22.1 ± 3.3	2180 ± 506
20	0.56 ± 0.01 ^b	18.6 ± 3.5	2808 ± 842	1341 ± 13	22.4 ± 4.3	2029 ± 609

The theoretical value of χ is 0.58 ± 0.05 ppm and the cross-sectional area is 19.0 ± 0.2 mm². The first column lists the echo time. The second and the sixth columns list χ solved from Eq. (13). The chosen radius, R , for solving Eq. (13) is 3.0 mm. The superscripts, a and b , refer to the two echo times used for quantifying susceptibility values. The third and seventh columns list the cross-sectional area of the cylinder calculated from Eq. (8). The fourth and eighth columns list the effective spin density inside the object calculated from the imaginary part used in Eq. (8). The fifth and ninth columns list the effective spin density outside the object.

^a T_E = 11 ms and 17 ms.

^b T_E = 11 ms and 20 ms.

Table 8
Quantified results from phantom images of the 128×128 matrix size reduced from slices shown in Table 7.

T_E (ms)	Slice number 12			Slice number 16		
	χ ppm	A_0 mm ²	$\rho_{0,c}$	ρ_0	χ ppm	A_0 mm ²
11		4.55 $\pm$ 0.32	10444 $\pm$ 835	5095 $\pm$ 51		4.52 $\pm$ 0.32
17	0.55 $\pm$ 0.02 ^a	4.83 $\pm$ 1.30	8729 $\pm$ 2008	4764 $\pm$ 48	0.55 $\pm$ 0.01	4.68 $\pm$ 1.26
20	0.56 $\pm$ 0.01 ^b	3.53 $\pm$ 1.73	12936 $\pm$ 4916	4664 $\pm$ 47	0.56 $\pm$ 0.01	3.53 $\pm$ 1.73

The meaning of each column has been explained in Table 7. The chosen radius, R, for solving Eq. (13) is 2.0 mm in these cases. The theoretical cross-sectional area is 4.75 $\pm$ 0.05 mm².

^a T_E = 11 ms and 17 ms.

^b T_E = 11 ms and 20 ms.

Table 9
Quantified results from phantom images of the 100×100 matrix size reduced from slices shown in Table 7.

T_E (ms)	Slice number 12			Slice number 16		
	χ ppm	A_0 mm ²	$\rho_{0,c}$	ρ_0	χ ppm	A_0 mm ²
11		2.96 ± 0.33	16241 ± 1949	8971 ± 88		3.02 ± 0.33
17	0.56 ± 0.03 ^a	2.96 ± 1.80	15433 ± 5093	8695 ± 87	0.56 ± 0.03	2.96 ± 1.80
20	0.56 ± 0.01 ^b	2.60 ± 1.80	18198 ± 8917	8631 ± 86	0.56 ± 0.01	2.84 ± 1.96

The meaning of each column has been explained in Table 7. The chosen radius, R, for solving Eq. (13) is 1.5 mm in these cases. The theoretical cross-sectional area is 2.90 ± 0.03 mm².

^a T_E = 11 ms and 17 ms.

^b T_E = 11 ms and 20 ms.