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A modulated closed form solution for quantitative susceptibility mapping — A thorough evaluation and comparison to iterative methods based on edge prior knowledge

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ABSTRACT

The aim of this study is to perform a thorough comparison of quantitative susceptibility mapping (QSM) techniques and their dependence on the assumptions made. The compared methodologies were: two iterative single orientation methodologies minimizing the l2, l1TV norm of the prior knowledge of the edges of the object, one over-determined multiple orientation method (COSMOS) and a newly proposed modulated closed-form solution (MCF). The performance of these methods was compared using a numerical phantom and in-vivo high resolution (0.65 mm isotropic) brain data acquired at 7 T using a new coil combination method. For all QSM methods, the relevant regularization and prior-knowledge parameters were systematically changed in order to evaluate the optimal reconstruction in the presence and absence of a ground truth. Additionally, the QSM contrast was compared to conventional gradient recalled echo (GRE) magnitude and R2* maps obtained from the same dataset. The QSM reconstruction results of the single orientation methods show comparable performance. The MCF method has the highest correlation ($corr_{MCF} = 0.95$, $r^2_{MCF} = 0.97$) with the state of the art method (COSMOS) with additional advantage of extreme fast computation time. The L-curve method gave the visually most satisfactory balance between reduction of streaking artifacts and over-regularization with the latter being overemphasized when the using the COSMOS susceptibility maps as ground-truth. R2* and susceptibility maps, when calculated from the same datasets, although based on distinct features of the data, have a comparable ability to distinguish deep gray matter structures.

Introduction

Phase imaging has shown over the last decade to offer a good contrast, both between and within brain tissues in respect to the conventional magnitude signal (Duyn et al., 2007; Rauscher et al., 2005) as well as veins and iron rich regions (Haacke et al., 2004). The effect observed in the phase is known to be non-local, it reflects the magnetic field induced by the tissues' magnetic susceptibility (Marques and Bowtell, 2005), which scales linearly with the increase of the fields strength (making it suitable at high field strengths).

Several studies have been performed on the origin of the susceptibility contrast with the main modulators being iron and myelin. Iron contributes to tissue contrast especially in the deep gray matter (globus pallidus, putamen and caudate) which has histologically derived high iron concentration showing good correlation with phase and susceptibility contrast (Bilgic et al., 2012; Schweser et al., 2011; Wharton and Bowtell, 2010). The other proposed contributor to the phase contrast, particularly between white and gray matter, is myelin where pathological demyelination has shown a decreased phase contrast between gray and white matter (C. Liu et al., 2011; Lodygensky et al., 2012) and good correlation was found between myelination and phase contrast during development. (Lodygensky et al., 2012).

In addition to the non-local effects associated with magnetic susceptibility, the chemical shift of water affected by macromolecules has been proposed to influence the measured phase (Luo et al., 2010; Shmueli et al., 2011; Zhong et al., 2008). More recently it was proposed (He and Yablonskiy, 2009) and demonstrated (Luo et al., 2013; Wharton and Bowtell, 2013; Yablonskiy et al., 2012) that the microstructural compartmentalization in the organization of lipids on the cellular and subcellular level (e.g. lipids, proteins) has a dominant effect on the contrast observed between white and gray matter in phase imaging.

Nevertheless, despite the last two effects being ignored when doing quantitative susceptibility mapping (QSM), this technique has demonstrated remarkable robustness in the ability to map iron deposition in

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deep gray matter structures (Langkammer et al., 2012; Schweser et al., 2011; Wharton and Bowtell, 2013). However, this problem is known to be ill-posed, and many methodologies have been suggested in order to better condition this problem. To make the problem over-determined, field maps of the object have to be measured with the object positioned in different orientations in respect to the magnetic field (Liu et al., 2009). This method is not practical for clinical studies, due to the increased measurement time and not applicable to subjects with reduced mobility. For these reasons many methods have been proposed using single orientation field maps together with additional regularization which can be broadly fitted in two classes: (*i*) correction of the k-space regions responsible by the artifact; (*ii*) prior-knowledge based on assumptions of smoothness and boundaries of the resulting QSM in the real space.

In the first class can be found direct methods that modify the kernel in a certain region which are responsible for the ill-conditioned nature of QSM (Schäfer et al., 2009; Schweser et al., 2013; Shmueli et al., 2009; Wharton and Bowtell, 2010), and the iterative methods that only use prior knowledge or sparsity constraints (l1 or TV norm) to reconstruct the ill-conditioned points while trusting the remaining k-space with (Schweser et al., 2012) or without different weighting in the transition regions (Wu et al., 2012). Alternatively, in the second approach (ii), the whole k-space is affected by the introduced prior knowledge. The susceptibility calculation can be done by minimizing the l2 norm in real space field generated by the susceptibility map and the measured field maps together with additional regularization based on prior knowledge with either the l2 norm (de Rochefort et al., 2010) (see l2 regularized single-orientation method) or the l1 norm (Kressler et al., 2010; T. Liu et al., 2011) (see l1 total variation denoising method). The prior information is extracted from the phase and magnitude maps assuming them to have similar edges of the underlying brain structure or simply assuming that natural images are sparse in some basis set. Recently, it was noted that this could be performed as a direct inversion when assuming smoothness of the susceptibility map (Bilgic et al., 2013) (see Modulated closed form solution).

The aim of the present study was to perform a thorough comparison of some of these methods (de Rochefort et al., 2010; Liu et al., 2009; T. Liu et al., 2011) and a newly proposed methodology dubbed modulated closed form (MCF) both in simulations and in in-vivo data. Particularly we accurately evaluate the impact of the prior information and of the regularization parameters and how their optimality can be evaluated in the absence of ground truth. Additionally, the susceptibility results were compared to R_2^* contrast in both the contrast between gray and white matter, deep gray matter and ability to detect multiple sclerosis lesions.

Theory

The magnetic susceptibility, χ, describes the reaction of a material to the presence of an external magnetic field. The magnetic field perturbation δB generated by a distribution of small magnetic susceptibility under a constant external magnetic field aligned to the z-direction, B_0, is given by a convolution of χ with the projection of the dipole field along the z-direction, D (Marques and Bowtell, 2005; Salomir et al., 2003). In the Fourier domain this can be simplified into a simple local expression:

$$\delta B(k) = D(k) \cdot \chi(k) \tag{1}$$

Where k are the k-space coordinates and the magnetic dipole kernel can be written in k-space as

$$D(k) = \frac{-k_x \sin\theta - k_y \cos\theta \sin\varphi - k_z \cos\theta \cos\varphi}{\|k\|} + 1/3 \tag{2}$$

Where θ describes the angle of rotation around the x-axis and φ the angle of rotation around the y-axis. These angles characterize the orientation of the externally applied magnetic field, B_0, in respect to the z-direction of the object.

The dipole kernel in k-space has zero elements located in two conical surfaces. These surfaces lie at the magic angle direction in respect to the main magnetic field orientation. This means that the same field perturbation can be generated by a large number of different susceptibility distributions. As a consequence the direct inversion of Eq. (1) is an ill posed problem and noise in the measured field, $\delta B(r)$, gets significantly amplified in k-space regions close to the two surfaces, leading to streaking artifacts in the reconstructed susceptibility maps.

In the following subsections a detailed description of the methods evaluated to overcome the ill posed nature of QSM will be given.

Multiple orientation method — COSMOS

Calculation Of Susceptibility through Multiple Orientation Sampling (COSMOS) takes advantage from the observation that the zero surface of the dipole kernel rotates with the magnetic field orientation B_0 (Liu et al., 2009; Marques and Bowtell, 2005). Hence the straightforward methodology to overcome the ill posed nature of QSM implies the measurement of the field perturbation with the object oriented in various directions in respect to B_0 (Liu et al., 2009; Marques and Bowtell, 2005). The χ map can then be calculated iteratively using a least squares conjugate gradient algorithm that minimizes,

$$min_\chi \sum_{i=1}^{N} \|M\left(F^H D_i(k) F\chi(\mathrm{r}) - \delta B_i(r)\right)\|_2^2 \tag{3}$$

where D_i and $\delta B_i(r)$ denote the dipole kernel and field perturbation for a specific object position, *i* indexes the multiple object orientations, *F* represents the Fourier Transform. M is a spatial mask that represents the regions inside the brain and is further modulated by a weighting term that guarantees that the noise throughout the field is equalized.

l_2 regularized single-orientation method

In the case where it is only possible to measure the field perturbation with the object positioned along one single orientation, extra information has to be introduced in the process of calculating the χ map. It is fair to assume that (i) the χ maps vary smoothly within anatomical boundaries/different tissue regions and (ii) that the artifacts, which are caused by the missing information around the magic angles, have structured sharp edges which cannot be found in the corresponding magnitude image. Consequently, regularization based on the l2 norm of the gradient has been widely promoted to tackle this problem (de Rochefort et al., 2010). As both the magnitude and the phase image images (Schweser et al., 2012) are expected to have similar edges as the underlying susceptibility distribution, they can be used as additional information to avoid the smoothing of the χ distribution close to tissue boundaries.

The regularized single-orientation (RSO) method incorporates prior knowledge of the expected edges by solving the following minimization problem using a least-squares conjugate gradient algorithm

$$min_\chi \|M\left(F^H D(k) F\chi(\mathrm{r}) - \delta B_0(r)\right)\|_2^2 + \beta \|M M_\nabla \nabla\chi(\mathrm{r})\|_2^2 \tag{4}$$

where the first term minimizes the distance between the estimated and measured field and the second term is the regularization prior tuned by a parameter β. The regularization term is a pixel by pixel multiplication of gradient of the susceptibility by a mask, M_∇, containing prior information regarding the regions where the gradients along a Cartesian direction are expected ($M_\nabla = 0$) or not ($M_\nabla = 1$). Both the regularization parameter and the gradient mask definition have a strong impact on the calculated χ map, the calculation of the latter will be discussed in the methods sections.