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Technical Note

Fast quantitative susceptibility mapping using 3D EPI and total generalized variation

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ABSTRACT

Quantitative susceptibility mapping (QSM) allows new insights into tissue composition and organization by assessing its magnetic property. Previous QSM studies have already demonstrated that magnetic susceptibility is highly sensitive to myelin density and fiber orientation as well as to para- and diamagnetic trace elements. Image resolution in QSM with current approaches is limited by the long acquisition time of 3D scans and the need for high signal to noise ratio (SNR) to solve the dipole inversion problem.

We here propose a new total-generalized-variation (TGV) based method for QSM reconstruction, which incorporates individual steps of phase unwrapping, background field removal and dipole inversion in a single iteration, thus yielding a robust solution to the reconstruction problem. This approach has beneficial characteristics for low SNR data, allowing for phase data to be rapidly acquired with a 3D echo planar imaging (EPI) sequence. The proposed method was evaluated with a numerical phantom and in vivo at 3 and 7 T.

Compared to total variation (TV), TGV–QSM enforced higher order smoothness which yielded solutions closer to the ground truth and prevented stair-casing artifacts. The acquisition time for images with 1 mm isotropic resolution and whole brain coverage was 10 s on a clinical 3 Tesla scanner.

In conclusion, 3D EPI acquisition combined with single-step TGV reconstruction yields reliable QSM images of the entire brain with 1 mm isotropic resolution in seconds. The short acquisition time combined with the robust reconstruction may enable new QSM applications in less compliant populations, clinical susceptibility tensor imaging, and functional resting state examinations.

Introduction

Quantitative susceptibility mapping (QSM) measures a fundamental physical property in vivo that is highly sensitive to tissue molecular composition and disease-induced tissue damage (De Rochefort et al., 2010; Marques and Bowtell, 2005; Shmueli et al., 2009). The clinical value of QSM has not yet been fully explored but holds great promise for vascular, inflammatory and neurodegenerative diseases of the brain (Wang and Liu, 2014).

To date, QSM has been shown to differentiate micro-bleeds from calcifications which otherwise appear similar on T2*-weighted images (Kaaouana et al., 2014; Liu et al., 2011b; Schweser et al., 2010a). QSM allows better delineation of deep brain structures from adjacent tissue than T2*-weighted images (Deistung et al., 2013; Eskreis-winkler et al., 2013; Schäfer et al., 2012); can be used to assess myelin content and the extent of loss during demyelination (Argyridis et al., 2013; Stüber et al., 2014; Wharton and Bowtell, 2014); and has the potential to map oxygen saturation along venous vasculature (Fan et al., 2013). Due to the strong paramagnetic effect of iron, iron levels in gray matter can be measured accurately with QSM to enable more specific investigation of age-related and disease-induced iron deposition (Langkammer et al., 2012; Li et al., 2013; Sun et al., 2014). Iron accumulation has

Abbreviations: EPI, echo planar imaging; GRE, gradient recalled echo; QSM, quantitative susceptibility mapping; SHARP, sophisticated harmonic artifact reduction on phase data; TGV, total generalized variation; TV, total variation.

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also been linked to the molecular cascade underlying neurodegeneration, which is in line with recent findings of increased susceptibility in deep gray matter of patients with Parkinson's and Alzheimer's diseases (Acosta-Cabronero et al., 2013; Langkammer et al., 2014; Lotfipour et al., 2012; Raven et al., 2013). In multiple sclerosis studies, QSM has utility to detect tissue demyelination changes in early stages of the disease (Blazejewska et al., 2014; Langkammer et al., 2013; Rudko et al., 2014) and to monitor susceptibility in multiple sclerosis lesions that may indicate iron accumulation or demyelination (Chen et al., 2014; Eskreis-Winkler et al., 2014; Wiggermann et al., 2013; Wisnieff et al., 2014).

Three dimensional (3D) GRE sequences for clinical QSM studies require acquisition times of at least 5 min when resolutions of $1 \times 1 \times 2$ mm^3 or better are desired. A higher resolution comes at the cost of prolonged acquisition times, reduced SNR and a higher sensitivity to patient-induced motion artifacts. When performing QSM, artifacts may also arise from physiological fluctuations, motion and blood flow. Additionally, modulation of oxygenation levels and organ motion during respiration may affect QSM results (Wen et al., 2014).

Several strategies have been described to address these problems. To reduce movement artifacts with shorter acquisition times, previous work has adopted 2D instead of 3D readout strategies. Fast 2D acquisitions with echo planar imaging (EPI) have been demonstrated for functional QSM at 9.4 T (Balla et al., 2014) and single-shot 2D EPI has shown promise for rapid assessment of QSM at clinical field strengths (Sun and Wilman, 2014). 2D imaging can yield comparable SNR efficiency to 3D acquisitions due to sequence considerations, particularly in low-resolution acquisitions. However, for high-resolution isotropic imaging, the SNR benefit from 3D imaging can be substantial. Instead of 2D scans, we here propose to acquire phase data with a 3D echo planar imaging sequence (Poser et al., 2010). The MR acquisition of 3D EPI images with 1 mm isotropic resolution and whole brain coverage requires approximately 10 s on a clinical 3 Tesla system. This efficient acquisition can be combined with a robust TGV-based QSM algorithm which reconstructs susceptibility maps in a single integrated step that includes background phase removal and dipole inversion.

In summary, the specific contributions of this work are:

- Combination of rapid 3D EPI acquisition and integrated QSM reconstruction.
- Incorporating phase unwrapping, background field removal, and dipole inversion into a single integrated step, thereby obviating the need for parameter selection in background filtering.
- Use of TGV instead of TV penalty to avoid stair-casing artifacts.
- Making the source code freely available for reproducibility of the presented results.

Methods

Total generalized variation

Dipole inversion methods using total variation (TV) penalty have been proposed to reconstruct the underlying magnetic susceptibility distribution from gradient echo phase data (Bilgic et al., 2012; Khabipova et al., 2014; Liu et al., 2011a; Schweser et al., 2012). However, TV only takes the first derivative of the susceptibility distribution into account and does not enforce higher-order smoothness, resulting in so called staircase artifacts for images that are not piecewise constant. As an alternative, the total generalized variation (TGV) penalty shares convenient properties of the TV functional, but also promotes higher-order smoothness and therefore leads to more accurate solutions (Bredies et al., 2010; Yanez et al., 2013). Past applications of TGV in MRI include parallel imaging, diffusion tensor imaging and PatLoc reconstruction (Knoll et al., 2012, 2013; Valkonen et al., 2013), in particular the under-sampled reconstruction and denoising of MR images as shown in Fig. 1 (Knoll et al., 2011).

Because TGV is the semi-norm on a Banach space, reconstruction problems with TGV penalty can be solved with tools developed for convex optimization problems. The well-known TV semi-norm of an image, or in the present case the susceptibility distribution χ, is described as:

$$\mathrm{TV}(\chi) = \|\nabla\chi\|_M$$

where ∇ denotes the gradient and $\|\cdot\|_M$ the Radon norm (a generalization of the L^1-norm). The TGV functional (here defined as second order TGV^2) itself represents a minimization problem:

$$\mathrm{TGV}^2_{\alpha_1,\alpha_0}(\chi) = \min_w \ \alpha_1\|\nabla\chi - w\|_M + \alpha_0\|\varepsilon w\|_M.$$

Minimization is performed over all vector fields w, where ε denotes the symmetrized derivative for vector fields resulting in second-order symmetric tensor fields, $\varepsilon w = \frac{1}{2}(\nabla w + \nabla w^T)$. For example, the symmetrized derivative ε for the 2 dimensional case is defined as:

$$w = \begin{pmatrix} w_1 \\ w_2 \end{pmatrix}, \ \varepsilon w = \begin{pmatrix} \frac{\partial w_1}{\partial x} & \frac{1}{2}\left(\frac{\partial w_1}{\partial y} + \frac{\partial w_2}{\partial x}\right) \\ \frac{1}{2}\left(\frac{\partial w_1}{\partial y} + \frac{\partial w_2}{\partial x}\right) & \frac{\partial w_2}{\partial y} \end{pmatrix}.$$

Second-order TGV^2 inherently balances locally the first and the second derivative of a function, as determined by the ratio of the positive weights α_1 and α_0. Note that the ratio of α_1 and α_0 has been experimentally shown to be ideal for MR images between 2:1 and 3:1 and therefore no additional parameter is introduced (Knoll et al., 2011). For all data presented in this work, the ratio of α_1 and α_0 was fixed to 3:1 and the reconstruction parameters for the 1 mm isotropic 3D EPI data were then empirically evaluated within a range of two orders of magnitude (α_0 from 0.0001 to 0.01). The visually obtained optimum value pair of $\alpha = (\alpha_1, \alpha_0) = (0.0015, 0.0005)$ was utilized in this work.

Integrative QSM reconstruction using TGV

As QSM reconstruction usually involves multiple steps, errors may propagate in each step, e.g. the error from the background phase removal directly impacts the result of the dipole inversion. Our approach instead acts directly on the wrapped phase data and incorporates the background field removal by introducing an auxiliary variable in the iterative regularization process for the dipole inversion. Furthermore, in comparison to other methods such as SHARP (Schweser et al., 2010b), no threshold parameter has to be defined for background field removal.

QSM maps were recovered from the wrapped phase of single gradient echo data $\phi_{wrapped}$. The recovery bases on an optimization procedure which operates on the Laplacian Δ of the unwrapped phase ϕ. The data $\Delta\phi$ can be obtained from $\Delta\phi_{wrapped}$, as described in (Schofield and Zhu, 2003), a technique which was first applied to QSM in (Li et al., 2011b; Schweser et al., 2013):

$$\Delta\phi = \mathrm{Im}\left(\Delta e^{j\phi_{wrapped}} \cdot e^{-j\phi_{wrapped}}\right).$$

The dipole inversion is implemented directly on the Laplacian of the phase:

$$\frac{1}{3}\frac{\partial^2\chi}{\partial x^2} + \frac{1}{3}\frac{\partial^2\chi}{\partial y^2} - \frac{2}{3}\frac{\partial^2\chi}{\partial z^2} = \frac{1}{2\pi T_E \gamma B_0}\Delta\phi \ \text{for the susceptibility} \ \chi.$$

Here, the background field was implicitly incorporated by the introduction of an auxiliary variable ψ whose Laplacian is required to be equal to the discrepancy of this equation on the brain mask Ω. This auxiliary variable was penalized by a squared L^2-norm, i.e., integrating its