Published in final edited form as:

Magn Reson Med. 2015 June ; 73(6): 2100–2110. doi:10.1002/mrm.25328.

Joint estimation of chemical shift and quantitative susceptibility mapping (chemical QSM)

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Abstract

Purpose—The purpose of this work is to address the unsolved problem of quantitative susceptibility mapping (QSM) of tissue with fat where both fat and susceptibility change the MR signal phase.

Methods—The chemical shift of fat was treated as an additional unknown and was estimated jointly with susceptibility to provide the best data fitting using an automated and iterative algorithm. A simplified susceptibility model was used to calculate an updated value of the chemical shift based on the local magnetic field in each iteration. Numerical simulation, phantom experiments and in vivo imaging were performed. Artifacts were assessed by measuring the susceptibility variance in uniform regions. Accuracy was assessed by comparison with ground truth in simulation, and using a susceptibility matching approach in phantom.

Results—Using the proposed method, artifacts on the QSM image were markedly suppressed in all tested datasets compared to results generated using fixed chemical shifts. Accuracy of the estimated susceptibility was also improved in numerical simulation and phantom experiments.

Conclusion—A joint estimation of fat content and magnetic susceptibility using an iterative chemical shift update was shown to improve image quality and accuracy on QSM images.

Keywords

Quantitative susceptibility mapping (QSM); water/fat separation; chemical shift; breast imaging

INTRODUCTION

Quantitative susceptibility mapping (QSM) in MRI has received increasing clinical and scientific interest (1–14). QSM contrast originates from the magnetic moments of the electrons orbiting around the nuclei in a molecule, and provides a valuable venue to exploit the full utility of the usually discarded phase images in MRI. It has shown promise in characterizing and quantifying molecular compositions such as iron, calcium, and gadolinium, making it relevant to the diagnosis and treatment of various neurological disorders (15–26).

Most of the existing QSM methods assume that susceptibility is the only contributor to the field inhomogeneity, which may be a valid assumption for applications in neuroimaging. However, the same orbiting electron cloud response to B_0 in molecules also magnetically shields the nuclei inside the electron cloud (27–29). The shielded protons in the molecule have a resonance frequency different from that of the unshielded ones, and this resonance frequency offset is referred to as chemical shift (30). This chemical shift affects the complex MRI signal, particularly the signal phase, because the shielded protons contribute to signal generation as well. Although estimation of the field inhomogeneity in the presence of chemical shift has been proposed in various algorithms such as Iterative Decomposition of water and fat with Echo Asymmetry and Least squares estimation (IDEAL)(31–32), these algorithms typically assume that the chemical spectrum is known *a priori*. Since the chemical spectrum may vary between subjects or even between organs within the same subject due to the differences in lipid compartmentalization and fatty acids content (33–34), the assumed chemical spectrum may not be accurate enough for the subsequent determination of susceptibility. Moreover, even using multi-peak models, ambiguity exists in how to assign the main components of the spectrum: the location of the central line (containing 60–85% of the overall fat signal) reported in the literature varies within a 0.2 ppm range (35–37). Another factor is the temperature dependence of the fat chemical shift (38). The underdetermined chemical spectrum adds another layer of numerical difficulty for faithful field map estimation in water/fat separation.

In this work, we present an automated joint estimation of the chemical shift and the susceptibility from an MRI dataset, where the chemical shift is also treated as an unknown variable subject to optimization. We refer to this method as chemical QSM. Through simulations, phantom validation, and in vivo data, it is demonstrated that this method yields higher quality QSM images, and enables QSM applications beyond neuroimaging.

THEORY

The field inhomogeneity in MRI can be measured using a multi-echo gradient echo sequence (7,39). The reconstructed image signal s of a voxel at a spatial location $\mathbf{r}$ measured at the m th echo time TE_n may be expressed as:

$$s(\mathbf{r}, TE_n) = e^{-i2\pi f_s(\mathbf{r})TE_n} e^{-R_2^*(\mathbf{r})TE_n} \sum_{k=0}^{m-1} \rho_k(\mathbf{r}) e^{-i2\pi f_k TE_n} \quad [1]$$

where $f_s(\mathbf{r})$ is the spatially varying field induced by the susceptibility referred to as susceptibility field, $R_2^*(\mathbf{r})$ is the apparent transverse relaxation rate for the voxel, m is the number of chemical species present in the voxel, f_k is the chemical shift constant of the k th species, and $\rho_k(\mathbf{r})$ is the contribution of the k th species to the complex signal of the voxel at $TE = 0$. After excitation, the signal experiences dephasing due to the chemical shift and the susceptibility field. For simplicity, the spatial index ($\mathbf{r}$) of any scalar field will be dropped hereafter whenever clarity is not affected. Each species is characterized by two parameters: ρ_k and f_k . The parameters of different species may be independent, such as water and fat, or correlated, such as different components of fat. In the scenario where only water $\{\rho_0, f_0\}$ and a single fat peak $\{\rho_1, f_1\}$ are present, Eq. 1 becomes:

$$s(TE_n) = e^{-i2\pi f_s TE_n} e^{-R_2^* TE_n} (\rho_0 + \rho_1 e^{-i2\pi f_1 TE_n}) \quad [2]$$

Here, we assumed that the chemical shift of water is zero: $f_0 = 0$ as the water resonance frequency is used as the reference frequency, such that any deviation is absorbed into f_s .

Challenges in previous attempts for estimating f_s

Previous algorithms estimate f_s and $\{\rho_k\}_{k=0,1}$ by assuming f_k is known *a priori* and minimizing a cost function that is the residual between the modeled and the measured signals over N different TEs:

$$f_s^*, R_2^{*}, \{\rho_k^*\}_{k=0,1} = \underset{f_s, R_2^*, \{\rho_k\}_{k=0,1}}{\operatorname{argmin}} \sum_{n=1}^N \|s(TE_n) - e^{-i2\pi f_s TE_n} e^{-R_2^* TE_n} (\rho_0 + \rho_1 e^{-i2\pi f_1 TE_n})\|_2^2 \quad [3]$$

The fat frequency f_1 is often assumed to be between -3.5 and -3.4 parts per million (ppm) (35–37,40). The uncertainty in the fat chemical shift has a substantial effect on the estimation of f_s^* , the inhomogeneity field map. This can be best understood by examining the signal behavior in a voxel consisting of fat only, where Eq. 3 reduces to the following:

$$f_s^* = \underset{f_s}{\operatorname{argmin}} \sum_{n=1}^N \|s(TE_n) - |s(TE_n)| e^{-i2\pi(f_s + f_1) TE_n}\|_2^2 \quad [4]$$

Here any error f_1 in the presumed chemical shift f_1 enters into the estimate f_s^* , because the cost function only depends on the sum of f_s and f_1 . As the susceptibility under investigation is often on the order of 0.01ppm to 0.1ppm(4), a 0.1 ppm error in the field map is very large and complicates a meaningful measurement of susceptibility. Therefore, it is desirable to treat f_1 as an additional unknown variable to be optimized.

To formulate the problem where the chemical shift frequencies f_j is treated as an additional unknown, the following energy function is minimized:

$$f_s^*, R_2^{*}, f_1^*, \{\rho_k^*\}_{k=0,1} = \underset{f_s, R_2^*, f_1, \{\rho_k\}_{k=0,1}}{\operatorname{argmin}} \sum_{n=1}^N \|s(TE_n) - e^{i2\pi f_s TE_n} e^{-R_2^* TE_n} (\rho_0 + \rho_1 e^{-i2\pi f_1 TE_n})\|_2^2. \quad [5]$$

This is a high dimensional non-linear data fitting problem. It is possible to solve it by discretizing f_1 , solving Eq. 3 for all voxels for a fixed f_1 , and selecting the f_1 with minimal

energy. However, this brute force search is computationally intensive and the precision is still subject to the discretization error in f_1 . Additionally, solving Eq. 3 for all voxels often involves smoothness assumption on f_s^* , which is not desirable for QSM. Instead, f_s^* is assumed to be generated by a physical susceptibility distribution according to the dipole convolution $f_s = d * \chi$, where d is the field of a unit dipole and χ is the susceptibility distribution (2,41–42). When a non-dipole field exist in f_s , the mismatch between model and the input data f_s , leads to streaking artifacts in the reconstructed susceptibility map. The typical streaking artifacts can be found algorithmically by detecting spurious edges that do not correspond to any anatomical features found in the magnitude image or in the T1 & T2 weighted images acquired in the same subject (8). The anatomical features can be represented in various mathematical forms, such as edges. The correct f_s would have minimal artifacts. The mathematical formulation used in this work is:

$$f_1^*, \chi^* = \underset{f_1, \chi}{\operatorname{argmin}} \lambda \sum_{n=1}^N \|s(TE_n) - e^{-i2\pi d * \chi TE_n} e^{-R_2^* TE_n} (\rho_0 + \rho_1 e^{-i2\pi f_1 TE_n})\|_2^2 + |MG\chi|, \quad [6]$$

where ρ_0 and ρ_1 may be treated as variables depending on the susceptibility field $d * \chi$ and chemical shift f_1 through variable projection (VARPRO)(37), G is the 3D gradient operator, M is an edge mask derived from the gradient of an anatomical prior obtained from the same MRI dataset (8), and λ is the Lagrangian multiplier whose value may be determined using Morozov's discrepancy principle (43).

METHODS

Iterative correction of the fat chemical shift

To avoid the brute force search over f_1 , this highly nonlinear and multidimensional problem defined by Eq. 6 was solved iteratively by performing a susceptibility calculation at only a few selectively updated f_1 values through the following approximation. It has been shown that water and fat have a susceptibility difference around 0.6ppm, which is much greater than susceptibility variations (0.01ppm~0.1ppm) reported in normal tissue (8). Thus, the susceptibility map was approximated to have two types of major sources, namely, water and fat, each having a constant but unknown susceptibility. This model was fit against the susceptibility field map estimated by a multi-echo Dixon water/fat separation method assuming a fixed chemical shift. Then any systematic discrepancy between the modeled and estimated susceptibility field map allows us to correct the chemical shift. Consequently, the reconstruction is split into two stages. In the first stage, we correct the presumed chemical shift based on the piecewise constant model introduced above. In the second stage, we removed the piece-wise constancy constraint to allow per-voxel susceptibility mapping. A flowchart of the method is presented in Fig. 1, where images are from an actual phantom (see the lard experiment section below). The specific implementation of each step is as follows.

Step 0: As one of the cornerstones of the algorithm, the T2*-IDEAL algorithm (32) was used for the mapping of water, fat and susceptibility field. Since the nonlinear minimization performed in IDEAL may converge to a local minimum, it is important to select an initial susceptibility field that is reasonably close to the true solution. Here, we

used the observation that the susceptibility field measured in MRI is typically dominated by the background field(13,44), which was defined here as the field generated by sources of susceptibility outside the region of interest. An important example of this is the air-tissue interface, which represents a susceptibility shift of around 9ppm. In QSM, it is necessary to estimate the background field such that the local field can be obtained, defined here as the field generated by sources of susceptibility inside the region of interest. Consequently, the relationship was written as $f_s = f_B + f_L$, with f_B and f_L the background and local field, respectively. Several algorithms have been developed to separate the background field f_B from f_L (13,44). Since we assumed that $f_L \ll f_B$, we used the obtained background field f_B as the initial susceptibility field for the T2*-IDEAL algorithm.

Before background field estimation was carried out, a preliminary field map was estimated assuming a single species. Using the finding that discontinuities between neighboring voxels on this preliminary field map were generally caused by either the limited dynamic range determined by the finite echo spacing TE , or the chemical shift f_1 , these discontinuities were removed by unwrapping field jumps $n/\Delta TE + m f_1^0$, where $n/\Delta TE$ is the standard 2π wrap-around with n an integer, and $m f_1^0$ is the chemical shift jump with $m=0$ or 1 . This unwrapping was performed with a magnitude-guided field unwrapping algorithm (45) and used an initial guess of the fat chemical shift value $f_1^0 = -3.5 \text{ ppm} \cdot \gamma B_0 \text{ Hz}$. The background field was then obtained by applying the projection onto dipole field (PDF)(44) method on the unwrapped field.

Step 1: In this step, an initial guess $f_1^{(k-1)}$ for the chemical shift was assumed and kept fixed. The water fraction map, defined as $\rho_0 / (\rho_0 + \rho_1)$, the fat fraction map, defined as $\rho_1 / (\rho_0 + \rho_1)$, and the susceptibility map $f_s^{(k)}$ were calculated using T2*-IDEAL (31). Note that no final smoothing of the field map $f_s^{(k)}$ was performed, in contrast to what is done conventionally.

Step 2: A local field $f_L^{(k)}$ was estimated from the susceptibility field $f_s^{(k)}$ again using the Projection onto Dipole Fields (PDF) method(44).

Step 3: Both water and fat were assumed to have constant, but unknown chemical shifts and magnetic susceptibilities. With this assumption, a previously reported piece-wise constant inversion of the magnetic field distribution (4,46) was implemented to estimate these susceptibilities and chemical shifts. The difference Δf_1 in the chemical shift between water and fat estimated in this step was then used to update the chemical shift of fat for the next iteration: $f_1^{(k)} = f_1^{(k-1)} + \Delta f_1^{(k)}$. The assumption that water and fat components have constant susceptibilities is not satisfied in general but is only made in this step to simplify the problem of the chemical shift update. This assumption is not made at the final susceptibility estimation step.

Step 4: steps 1–3 were repeated using the new chemical shift estimate $f_1^{(k)}$ until the chemical shift update $\Delta f_1^{(k)}$ was smaller than a certain preset threshold. Otherwise, the

field map $f_s^{(k)}$ was passed to the morphology enabled dipole inversion (MEDI) method (45) for per-voxel QSM.

Numerical phantom simulations

Two numerical phantoms with a $128 \times 128 \times 64$ matrix size were constructed to test the feasibility of the proposed approach and evaluate its performance in different conditions. For the first simulation, the phantom consisted of a centered $109 \times 109 \times 49$ voxel volume of water with an imbedded cylinder of fat with a diameter of 7 voxels, oriented perpendicularly to the main magnetic field B_0 ($B_0 = 3T$) (Fig. 2 A). The fat chemical shift was assumed to consist of a single peak at $f_1 = -3.60$ ppm, while its susceptibility was assumed to be 0.6 ppm. The background field was modeled as a linear gradient across the phantom. The second phantom consisted of $109 \times 109 \times 49$ volume of water centered in the field of view. It contained eight cylinders with different diameters (3, 7 and 10 voxels were used) each having a mixture of water and fat in different proportions, leading to 100%, 95%, 87.5%, 75%, 62.5%, 50%, 37.5% and 25% fat fractions. Fat was assumed to have a multi-peak spectrum with frequencies $f_k = \{-3.82, -3.46, -2.74, -1.86, -0.50, 0.53\}$ ppm and corresponding relative amplitudes $\alpha_k = 0.01 \{9.45e^{-i\pi 0.181}, 64.66, 9.67e^{i\pi 0.046}, 2.26e^{-i\pi 0.567}, 2.22e^{-i\pi 0.244}, 8.83e^{-i\pi 0.089}\}$. These relative amplitudes were reported in a previous study(35). All cylinders were oriented perpendicularly to the B_0 field ($B_0 = 3T$). The background field was modeled by imposing a linear field gradient across the phantom. The susceptibility of fat was still assumed to be 0.6 ppm. For both phantoms, MRI data was simulated using the following scan parameters: TE= 2.5ms, TE spacing TE=0.75ms, Number of echoes #TE=15, and voxel size = $1 \times 1 \times 1 \text{ mm}^3$. In all simulations, complex Gaussian noise was added to the signal, producing a peak signal-to-noise ratio (PSNR) of 30. The proposed algorithm – which assumed a single fat peak – used an initial guess of -3.46 ppm (main peak of the multi-peak spectrum) for the chemical shift $f_1^{(0)}$.

Lard phantom experiment

To validate the accuracy of estimated susceptibility using the proposed method, a phantom experiment was performed using a susceptibility matching approach as the reference standard. The phantom experiment was performed on a 3T MRI system (GE Excite HD, Milwaukee, WI) using an 8-channel head coil. The phantom consisted of a container filled with a known volume of water and a fixed stick of lard (Pinnacle Foods Group LLC, Parsippany, NJ). A series of acquisitions with identical scan parameters (TE = 2.7 ms, TE = 3.3ms, #TE = 8, TR = 29.4ms, FA = 15° , BW = $\pm 62.5 \text{ kHz}$) were performed. Between successive acquisitions, a solution with a fixed and known concentration of Gd was added to the water, thus gradually increasing the susceptibility of the water surrounding the lard. The range of obtained susceptibilities was between 0 and 0.5ppm, with a step size of 0.01ppm between 0.23ppm to 0.43ppm. Three analyses were performed:

- a. When the susceptibility of the water solution matched that of lard, no or very low variations of the local magnetic field are expected, since the characteristic paramagnetic dipole pattern of fat vanishes in this situation. This susceptibility match was found by computing the norm of the local magnetic field (obtained with linear fitting alone) outside the lard fat region and selecting the acquisition with the

smallest norm. The susceptibility of lard was then obtained by converting the Gd concentration in the phantom into susceptibility using the following formula:

$$\chi_{\text{solution}} = \chi_{\text{mol,Gd}} \cdot [\text{Gd}], \text{ where } \chi_{\text{mol,Gd}} \text{ is the molar susceptibility of Gd, } \chi_{\text{mol,Gd}} = 326 \text{ ppm/M.}$$

- b. For each acquisition, the lard susceptibility relative to the phantom Gd solution was obtained using a piece-wise constant method previously proposed (4), except for the background field removal step, which was performed using the projection onto dipole fields method. Gd concentrations were converted to susceptibility as in a).
- c. Finally, for each acquisition, a field map was obtained with the proposed method (using -3.46 ppm as an initial guess) and then used to reconstruct a susceptibility map using MEDI. The lard susceptibility relative to Gd solution was derived from the Gd concentration as in a).

Bovine tissue experiment

A piece of excised bovine tissue containing intramuscular fat was scanned on a 3T MRI system (GE Excite HD, Milwaukee, WI) using an 8-channel head coil. A multi-echo 3D SPGR sequence was used for data acquisition with imaging parameters: TE1=2.5ms,

TE=2.25ms, 7 echoes, 3 acquisitions with TE1 incremented by 0.75ms between acquisitions, TR=19ms, FA=20°, BW=±62.50 kHz, voxel size = $0.94 \times 0.94 \times 1 \text{ mm}^3$ and scan time ~9 minutes. The proposed algorithm was performed on the first 15 of the acquired echoes and used an initial guess of -3.46 ppm for the chemical shift $f_1^{(0)}$. We also performed the reconstruction using 6 of the acquired echoes with an echo spacing TE=3ms to test the robustness of the proposed technique with respect to the choice of echo spacing and echo number.

Volunteer breast scan

After obtaining informed consent, four female volunteers were scanned. All exams were performed under protocols approved by the Institutional Review Board. Images were obtained using a 3T MRI system (MAGNETOM Verio, Siemens Healthcare, Erlangen, Germany) using a 16 channels (8 channels per breast) breast coil (Invivo, Gainesville, FL). A multi-echo spoiled gradient echo sequence was used for the exams using the following imaging parameters: TE= 3.3ms, TE=3.3ms, #TE=8, TR=35ms, FA=20°, BW=±62.50 kHz, and voxel size = $1 \times 1 \times 1 \text{ mm}^3$. The proposed algorithm was performed on the resulting images and used an initial guess of -3.46 ppm for the chemical shift $f_1^{(0)}$.

Image processing and analysis

In the iterative correction of the fat chemical shift, a precision of 1 Hz was set as the convergence level for all the experiments. In the numerical simulations, where the ground truth was available, the improvements after the chemical shift correction were assessed by calculating the difference between the estimated (χ^*) and true (χ_0) susceptibility maps relative to the noise level. This measure was defined as

$$\|\chi^* - \chi_0\|_2^2 / \sigma^2 \quad [7]$$

where σ^2 is the expected energy of noise on the reconstructed susceptibility map. This value was estimated as $\sigma^2 \approx \|\chi_t - \chi_0\|_2^2$, where χ_t is the susceptibility map reconstructed from the noisy field map with the chemical shift fixed to its ground truth value. When the algorithm converges to the correct chemical shift, this measure should be 1.

For the phantom experiments, image artifacts were assessed by measuring the standard deviation of susceptibility values in uniform regions, such as the Gd solution region outside the lard in the lard experiment, and the muscle region in the bovine tissue experiment.

For in vivo experiments, fitting residuals

$$\text{Res}(f_1^{(k)}) = \sum_{n=1}^N \left\| s(TE_n) - e^{i2\pi f_s^{(k)} TE_n} e^{-R_2^* TE_n} (\rho_0^{(k)} + \rho_1^{(k)} e^{-i2\pi f_1^{(k)} TE_n}) \right\|_2^2 \quad [8]$$

were recorded, where $f_s^{(k)}$, $R_2^{*(k)}$, $\rho_0^{(k)}$ and $\rho_1^{(k)}$ were estimated from T2*-IDEAL(32) once $f_1^{(k)}$ was known.

RESULTS

Numerical experiments

In each case, the convergence of the updated chemical shift value was reached within 10 iterations. Reconstructed QSM maps are shown in Fig. 2. It can be noted that the one-peak model with the use of chemical shift correction was able to produce improved results compared to the non-corrected models (Fig. 2, B and C, F and G). Reconstruction of the single-peak phantom using the fixed one peak model (−3.46 ppm) resulted in a relative error of 1.656; the proposed chemical shift update, which converged to ≈ -3.6 ppm, led to an error reduction down to 1.01. Reconstruction of the multi-peak phantom using the fixed main peak model (−3.46 ppm) resulted in the relative error of 1.304, and proposed chemical shift update, which converged to −3.55 ppm, allowed to reduce this value to 1.01.

Fig. 3 shows a comparison of the local field maps estimated using the true multi-peak chemical spectrum, the fixed one peak model (main peak) and the proposed algorithm. The assumption of a fixed peak led to an absolute error on the order of 10 Hz in the fat region pointed by arrows. The proposed method reduced this error down to 1.5 Hz.

Finally, Fig. 4 shows a comparison between the true fat fraction map used in the numerical simulation and the fat fraction map estimated using the fixed main peak and using the proposed algorithm. The error in the voxels containing mixtures of species was around 10% both for the fixed model and the proposed method.

Lard phantom results

Results of the lard susceptibility matching measurement are shown in the Fig. 5. It was found that the norm of the local field was minimal when the susceptibility of the background

Gd solution was equal to 0.35 ppm (Fig. 5A). Results of the piece-wise estimation of the lard relative susceptibility are shown in Fig. 5B. The plot shows that the susceptibility difference between lard and the phantom background decreases linearly with increasing Gd concentration. The susceptibility of lard (0.37ppm) is obtained by taking the intercept of the linear fit of this data. Results of the susceptibility estimation using the proposed algorithm are shown in the Fig. 5C. For each acquisition, the chemical shift converged to a value of -3.65 ppm. Again, the estimated relative susceptibility of lard followed the same linear trend, with an intercept of 0.36 ppm.

The QSM and corresponding field maps without added Gd are shown in Fig. 6. A considerable reduction in streaking artifact was observed with the proposed method (Fig 6C, standard deviation outside lard was 0.01 ppm) compared to using a fixed chemical shift (Fig 6B, standard deviation outside lard was 0.05 ppm). The accuracy of the estimated susceptibility of lard was improved in the proposed method (0.35 ppm) compared to using a fixed chemical shift (0.27 ppm).

Bovine tissue experiment results

Fig. 7 shows a comparison of the QSM maps obtained for the bovine tissue scan without and with the use of the chemical shift update both for the 15 and 6 echo datasets. A marked reduction of streaking artifacts was noticed, with the standard deviation of the susceptibility values within a muscle region reduced from 0.27 to 0.12 ppm for the 15 echo data and from 0.26 to 0.15 ppm for the 6 echo data. Good visual agreement was observed between these two reconstructions with chemical shift update (Figs. 7C&E), although the SNR appeared to be higher in Fig. 7C that utilized more echoes. Overall improved preservation of the complex anatomical structure was observed in the updated chemical shift model, which converged to -3.6 ppm, compared to the fixed chemical shift reconstruction, which used -3.46 ppm).

Volunteer breast scan

Results of the breast QSM experiments are shown in the Fig. 8 and Fig. 9. Fig. 8 shows a comparison of the QSM maps obtained without (-3.46 ppm) and with using the proposed chemical shift update algorithm, which converged to -3.3 ppm, with the results of the mammography study. The detected hypointensities in the QSM image correspond to the hyperintensities in the x-ray image and were confirmed by an experienced radiologist (R.R.E.) to be calcifications.

Fig. 9 shows a comparison of the QSM maps obtained for the breast exam in a second subject without (-3.46 ppm) and with the use of the chemical shift update, which converged to -3.3 ppm. In QSM, a high susceptibility structure (~ 1.3 ppm) was identified, and was confirmed to be a biopsy clip. Fig. 10 shows the residual as a function of the chemical shift value for this data set, with each “+” representing consecutive steps of the proposed algorithm starting from an initial guess for f_1 that was intentionally set to -3.8 ppm.

DISCUSSION

In this article, a fully automated iterative algorithm for quantitative susceptibility mapping (QSM) within tissues with significant fat content has been presented. The algorithm assumes that the field inhomogeneity is caused by the susceptibility of two species – water and fat – and their chemical shifts. It utilizes the updated prior information about tissue structure and penalizes the discrepancy between modeled and measured signals. Simulations, phantom validation and in vivo results suggest that the proposed chemical shift correction effectively reduces streaking artifacts and preserves fine anatomical structures in the final QSM.

QSM involves solving an ill-posed inverse problem that is sensitive to error propagation, so it has a high accuracy requirement for the input field map. Taking the brain QSM as an example, the noise standard deviation on the estimated field map is on the order of $1/\text{SNR}/(2\pi\text{TE}) = 0.1\text{Hz}$ with $\text{SNR}=50$ assumed at $\text{TE}=30\text{ms}$. Although field map estimation may appear to be simple even in the presence of chemical shift, a straightforward application of T2^* -IDEAL proves to be insufficient to reach the accuracy level required for the field map, leading to substantial streaking artifacts. One key revelation here is that error in the presumed chemical shift (0.1ppm, translated to 6.4Hz at 1.5T or 12.7Hz at 3T) leads to a substantial error in the estimated field map as demonstrated by Eq. 4. It was shown in the experimental results that only the chemical shift resulting from an iterative data fitting procedure was able to reach the accuracy level of the field map required by QSM.

The uncertainty in the chemical shift has been reported in literature. Recent publications (35–37) demonstrate an increased interest in the multi-component modeling of the chemical shift. However, different fat components are generally assumed to be correlated with fixed relative amplitudes and spectral shifts, and ambiguity exists in how to assign the main components of the spectrum: the reported location of the central line (containing 60–85% of the overall fat signal) varies within a 0.2 ppm range (35–37). To obtain an accurate measurement of the chemical shift, additional NMR spectroscopy may be required. Nevertheless, there is evidence that fat may cause bulk magnetic susceptibility effects (47), shifting spectral components, and thus rendering ineffective otherwise precise spectral models. Depending on the fat compartmentalization, its resonance frequencies might shift depending on orientation relative to the direction of magnetic field, as suggested in references (33,47–48). Additionally, it is inconvenient or impossible to perform a spectroscopy for each individual subject or organ examined.

The uncertainty in chemical shift also causes errors in the water and fat fraction maps. However, it did not lead to substantial noticeable artifacts on the water and fat images. This robustness may be due to the fact that the off-resonance frequency is only used to demodulate the recorded MRI signal, which is followed by a well-posed least squares fitting problem to estimate ρ_0 and ρ_1 (31). In contrast, QSM, which requires solving an ill-posed inverse problem, is much more sensitive to inaccuracies. Errors in a single voxel may propagate to its surroundings, causing streaking artifacts. Therefore, the calibration of chemical shift appeared to be a critical step for QSM.

The proposed algorithm is useful in clinical and research applications where the knowledge of field distribution is crucial. The ability to calculate precise field distributions may be important for active shimming or MR-based thermography. Although only breast QSM is shown in this study, we expect the proposed algorithm will show similar improvements in other organs where chemical shift is present.

Further improvements of the current implementation are possible. Although multiple fat species can be handled as formulated in Eq. 1, the current implementation requires a segmentation of water region and fat region, which is automatically obtained using T2*-IDEAL. When multiple types of fat are imaged within the same FOV, the automatic segmentation of different types of fat may be challenging, considering that the frequency difference between them are small. However, if prior information is available on the locations of different types of fat, then the water/fat separation problem can be solved independently in different regions. This allows extending the proposed method to the case of multiple fat types. This limitation did not appear to have undermined the quality of reconstructed phantom and in vivo susceptibility maps presented in this work. This may be due to the fact that only a single type of fat was present within the FOV (e.g., lard or fatty breast tissue). Additionally, the assumption of a fixed fat spectrum across the FOV is made by most existing water/fat separation methods. In the numerical simulations, a single peak model was used to fit the data generated by a multi-peak spectrum, with minimal effect on the estimated field map accuracy. It is noted that the updated chemical shift is different from the main peak. Thus, the proposed algorithm finds an effective frequency which results in the lowest fitting residual. Regarding the imaging parameters, carefully chosen TEs may improve the SNR of the water and fat maps(49), which is useful for the automatic segmentation. In our experiments, bandwidth was on the order of 500Hz per pixel, corresponding to a shift of less than one voxel at 3T. Switching to lower bandwidth such as $\pm 16.25\text{kHz}$ would improve SNR, but at the expense of voxel shifts up to 4 voxels that would require further correction. Additionally, only a single R2* was assigned for each voxel, although water and fat may have different R2*. This limitation did not seem to have affected the reconstructed QSM images, which may be due to 1) most of the voxels contain a single species, and 2) R2*, which affects signal amplitude, has minimal effect on the field estimation step that mainly utilizes signal phase.

In conclusion, a joint estimation of fat content and magnetic susceptibility using a fully automated iterative chemical shift update is proposed. Numerical simulations, phantom and volunteer studies showed that the proposed iterative algorithm markedly reduced artificial signal variation on the QSM image and improved the accuracy of the estimated susceptibility in numerical simulation and phantom experiments.

Acknowledgments

This investigation was supported in part by grants R43EB015293-01A1 from National Institutes of Health.

Abbreviations

QSM quantitative susceptibility mapping

IDEAL	iterative decomposition of water and fat with echo asymmetry and least squares estimation
PDF	projection onto dipole fields
PSNR	peak signal-to-noise ratio
SPGR	spoiled gradient echo
MEDI	morphology enabled dipole inversion

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Fig. 1. Flowchart of the proposed algorithm. Symbols are defined in the text. Note that local field is updated at step 4 compared to step 2.

Fig. 2.

Results of the numerical experiments: comparison of QSM maps reconstructed using conventional T2*-IDEAL and proposed algorithm (first row: one-peak fat spectrum, second row: multi-peak fat spectrum). A, E: T2*-weighted images of the simulated phantoms. B, F: QSM images reconstructed from the susceptibility field f_s estimated with assumption of the chemical shift value $f_J = -3.46$ ppm. C, G: QSM images reconstructed from the susceptibility field f_s estimated with proposed iterative algorithm. H, I: Difference between QSM maps reconstructed from the susceptibility fields f_s estimated with proposed algorithm and the true susceptibility maps. Note that significant suppression of the streaking artifacts was achieved using the proposed algorithm in C and G.

Fig. 3.

Results of the numerical experiments: comparison of local field maps reconstructed using conventional T2*-IDEAL and proposed algorithm. A: local field map reconstructed with the true spectrum. B: local field map reconstructed with assumption of the chemical shift value $f_I = -3.46$ ppm. C: local field map reconstructed using the proposed algorithm. D, E: Difference between A and B, and A and C, respectively. It can be seen that frequency offset in regions with high fat content is reduced after correction of the chemical shift in C and E.

Fig. 4.

Results of the numerical experiments: comparison of fat fraction maps reconstructed with different assumed spectra. A: true fat fraction map. B: fat fraction maps reconstructed with assumption of the chemical shift value $f_I = -3.46$ ppm. C: fat fraction maps reconstructed using the proposed chemical shift update. D, E: Difference between A and B, and A and C, respectively. Both B and C showed similar fat fraction maps with respect to the truth.

Fig. 5.

Lard experiment. A: Dependence of the lard susceptibility field variation on the susceptibility of the Gd solution. B: Results of the piece-wise estimation of the lard susceptibility relative to the background solution for different concentrations of Gd. C: Results of the lard susceptibility using the proposed algorithm for different concentrations of Gd. The susceptibility values of lard estimated using three different techniques were in good agreement.

Fig. 6.

Reconstructed local field maps and QSM of the lard experiment. A, D: Magnitude image. B, E: QSM image reconstructed from the susceptibility field f_s estimated with assumption of the chemical shift value $f_l = -3.46$ ppm. C, F: QSM image reconstructed from the susceptibility field f_s estimated with proposed iterative algorithm. G, I: local field map corresponding to B, E, and H, J: the local field map corresponding to C, F. Images A–C, G, and H are coronal views. Images D–F, I, and J are sagittal views. Note the frequency offset in the lard region in the local field (G, I) and the resulting artifact in the susceptibility map (B, E) for the fixed chemical shift reconstruction. These are similar to those observed in numerical simulations in Fig. 3, and the artifacts are suppressed using the proposed algorithm as shown in C and F.

Fig. 7.

Results of the bovine tissue experiment: comparison of QSM maps reconstructed using conventional T2*-IDEAL and the proposed algorithm from 15 and 6 echo data. A: T2*-weighted image. B, D: QSM image reconstructed from the susceptibility field f_s estimated with assumption of the chemical shift value $f_I = -3.46$ ppm using 15 and 6 echoes, respectively. C, E: QSM image reconstructed using the proposed iterative algorithm using 15 and 6 echoes, respectively. F–I are the local fields corresponding to B–E, respectively. The proposed chemical shift update suppresses streaking artifacts for both datasets, although the use of more echoes resulted in a higher quality susceptibility map.

Fig. 8. Comparison of mammogram (A) with minimal intensity projections of breast QSMs reconstructed without (B) and with (C) the proposed algorithm. Arrows point to the detected calcifications, which are better seen in the map reconstructed with the proposed method as compared to that reconstructed with the fixed chemical shift reconstruction.

Fig. 9.

Results of a volunteer breast contrast exam (post Gd injection images are shown): comparison of QSM maps reconstructed using a fixed chemical shift (B) and the proposed algorithm (C). A T2*-weighted image (A) is provided as a reference. Arrows point to the location of a biopsy clip. Note the more homogeneous distribution of the fat susceptibility values and the brighter appearance of the metal object relative to fat after application of the chemical shift correction.

Fig. 10.

Model residual as a function of the chemical shift; the “+” symbols indicate the location of the successive iterations of the proposed algorithm for the data in Fig 9. This demonstrates that the proposed method finds the global minimum of the combined fat, water and chemical shift minimization problem.