

# A weighted gradient regularization solution to the inverse problem from magnetic field to susceptibility maps (magnetic source MRI): validation and application to iron quantification in the human brain

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## PURPOSE

Quantitative mapping of susceptibility in MRI has a wide range of biomedical applications, including molecular/cellular imaging, contrast-agent studies, fMRI BOLD quantification, and the assessment of iron overloading such as in neurodegenerative and brain vascular diseases. Susceptibility quantification using MRI has been sought after for a long time with various approaches (1-3). However, it is only recently that the feasibility of quantitatively mapping susceptibility has been experimentally demonstrated using the magnetic source MRI approach. This method inverts the local magnetic field (as measured from the MR signal phase) to the magnetic dipole source or susceptibility (4-8). This inversion from field to source is a challenging ill-posed problem (4) and adapting the data acquisition and/or regularizing the inversion is required to generate a reasonable solution (4-8). The regularization without the constricting acquisition is practically preferred, but previous approaches showed an important dependence on the regularization function. Here, a solution that makes use of the magnitude image gradient information is shown to be more accurate.

## THEORY

The forward problem from susceptibility source to magnetic field is given by  $B = C \otimes \chi$ , where  $B$  is the local field (along  $B_0$ ),  $C$  is the dipole convolution kernel  $[3 \cos^2(\theta) - 1]/4\pi|r|^3$  in image space or  $1/3 - k_z^2/k^2$  in Fourier space (2,3), and  $\chi$  is the susceptibility distribution. Here, the inverse problem for this convolution considers the background field induced by sources outside the FOV or resulting from shimming limitations by modeling it with a polynomial  $S\varepsilon$ . The formulation also takes into account the non-uniform noise of the MR signal phase. The resulting inverse problem with regularization can be written as:

$$\min_{\chi, \varepsilon} \|W(C\chi + S\varepsilon - B/B_0)\|_2^2 + \alpha \|M\chi\|_2^2 + \beta \|W_g G\chi\|_2^2$$

The first term is the squared distance between the measured field and the fitted one  $C\chi + S\varepsilon$ . It is weighted by  $W$  ( $W^2$  is the inverse of the phase noise correlation matrix), which is diagonal and proportional to the MR signal magnitude. The second and third terms are regularization terms on the susceptibility and its gradient, respectively.  $M$  is a mask defining a region at the domain boundaries (water/ background tissue) to force a reference region.  $W_g$  is the modulus of the inverse of the gradient of the MR signal intensity, which is used to impose edge information. This weighting results in a smoothing of the solution within regions with uniform MR signal intensity while allowing sharp transitions where magnitude varies. A conjugate gradient algorithm was used to perform the regularized inversion.

## MATERIAL AND METHODS

Experiments were performed at 1.5T (GE Healthcare, Waukesha, WI) using a 3D gradient echo sequence. In vitro, imaging was performed on a 12.5 cm diameter cylindrical phantom filled with water and balloons containing a range of gadolinium solutions that produce separate susceptibility regions ranging from 0 to 5 ppm with respect to water. Scanning parameters were: FOV = 128 mm, imaging matrix  $64^3$  isotropic resolution, bandwidth per pixel BW=1 kHz, TR=30 ms, TE=1.2, 2.2, 3.2, 4.2 and 5.2 ms, flip angle of 30°, and the body coil for signal reception. Field maps were calculated from the dephasing between echoes (4). The inversion procedure was performed on the phantom over a range of regularization parameters  $\alpha$  and  $\beta$ , with shim orders ranging from 0 to 4, and with and without the gradient weighting matrix to assess the influence of each parameter and to identify optimized inversion parameters.

Patients suffering from cerebral cavernous malformation with hemorrhages underwent Susceptibility Weighted Imaging from which data were retrospectively processed. Axial slices were acquired with FOV=24 cm, slice thickness 2 mm, matrix=512x384x32 (partial  $k_y=75\%$ ), BW=122 Hz, TR/TE=50/40 ms, flip angle=20° with an 8-channel surface coil. Raw reconstructed phase maps were unwrapped using region-growing and a susceptibility reconstruction using the parameters identified above, was performed on a limited region within the brain presenting important phase defects.

## RESULTS

With  $\alpha = 0$ , convergence is not obtained in 3000 iterations (IT, ~1s per IT). Increasing  $\alpha$  (Fig.1) allows converging in ~1000 IT but leads to limited image quality in the susceptibility map. Using a standard gradient-based regularization with  $\beta = 100$ , a solution is reached in ~100 IT but suffers from excessive smoothing and attenuation (Fig.2-d). The weighted gradient technique converges in ~1000 IT and provides an optimal susceptibility map both qualitatively and quantitatively, regardless on the value of  $\beta$  in the tested range (slope=0.97, Fig.2d). The result in Fig.2c shows complete removal of the streaking artifact, much better edges definition and limited attenuation of susceptibility values. In the brain data (Fig.3) a strong paramagnetic region with susceptibilities close to 1.2 ppm relative to tissue indicates a concentration of  $Fe^{3+}$  of 6.8 mM, consistent with Hb in blood, assuming a molar susceptibility of 177 ppm/M.

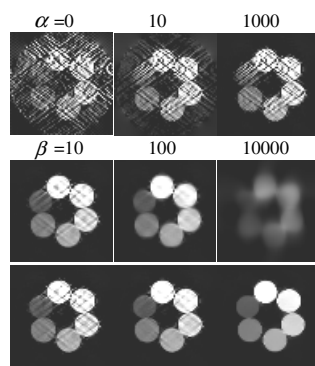


Fig.1 Top row from left to right: results for different  $\alpha$  ( $\beta = 0$ , shim order=0). Middle and bottom row for  $\alpha=1000$  and shim order=0: standard gradient regularization only smooths the solution as  $\beta$  increases (middle row) while the weighted-gradient solution preserves the edges (bottom row).

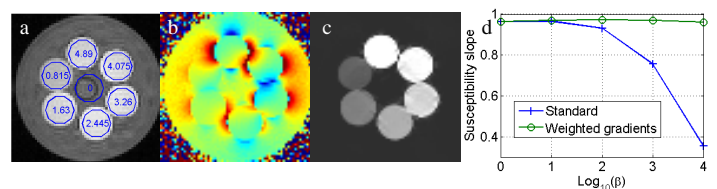


Fig.2 Phantom intensity (a) and phase (b) as well as reconstructed susceptibility map (c), weighted gradient method with  $\alpha = 1000$ ,  $\beta = 1000$ , shim order=0). d: susceptibility slope with standard and weighted gradient regularizations for a range of regularization parameters showing that the weighted gradient term provides good quantification for all tested  $\beta$ .

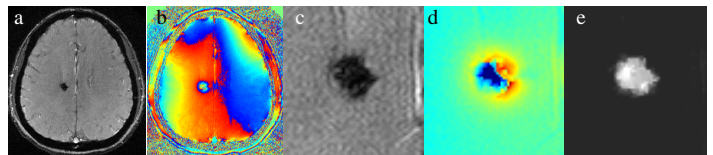


Fig.3 Brain intensity (a) and phase (b) on a hemorrhage. Zoom on the signal void (c) and unwrapped phase map (d). e: reconstructed susceptibility map.

## DISCUSSION AND CONCLUSION

Obtaining quantitative susceptibility maps from MR phase images with a single acquisition (6) requires the use of prior information or constraints. Boundary values need to be imposed for efficient convergence. This is done by defining the background at the domain boundaries. Using a gradient regularization stabilizes further the inversion and combined with edge priors available from the intensity image, it improves the quantification of susceptibility and image quality. This technique can be applied in vivo to quantify iron in hemorrhage which may be used for staging. It may also be applied to other diseases or situations that affect susceptibility such as calcifications and contrast agents.

## REFERENCES

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