A regularized k-space-based method for susceptibility tensor imaging

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INTRODUCTION: Recent studies showed that gradient-echo MRI derived brain white matter contrasts, including magnitude, phase, T_2^* and susceptibility are all dependent on fiber orientation (1-5). Particularly, tissue susceptibility is an intrinsic tissue property, of high contrast and SNR, and is related to the fiber angle with a simple sine-squared relationship (6). Hence, susceptibility provides a promising candidate for extracting white matter fiber orientation information from gradient echo MRI. Liu first demonstrated susceptibility tensor imaging (STI) of mouse brain (5). The application of STI reconstruction, however, can be hampered by imperfect registration due to different image distortion at different orientations. Since phase is usually strongest at the tissue boundaries, the imperfect registration of phase at tissue boundary can lead to significant artifacts in the resulting susceptibility tensors. In this work, a regularized k-space-based method for STI is proposed, which can effectively reduce the resulting errors due to imperfect image registration.

MATERIALS AND METHODS:

Human brain imaging: One healthy adult volunteer was scanned on a GE MR750 3.0 T scanner with a quadrature head coil. Gradient-echo images with 16 different head orientations were acquired using a standard flow-compensated 3D spoiled-gradient-recalled-echo (SPGR) sequence with the following parameters: TE = 40 ms, TR = 60 ms, flip angle = 20º, 2 mm isotropic resolution.

Mouse brain imaging: 3 perfusion-fixed (ProHance: formalin = 1:10, v:v) mouse brains were scanned using a 7.0 T magnet with a 3D SPGR sequence with FOV = 22x22x22 mm^3, matrix = 256x256x256, TE = 8.0 ms, TR = 50 ms, flip angle = 60º. A total of 15 to 19 orientations were sampled that roughly cover the spherical surface evenly.

STI reconstruction: Image phase was unwrapped using Laplacian-based phase unwrapping and converted to frequency shift (7). The background frequency was removed with a modified SHARP method (7, 8). In *k*-space, the normalized frequency shift, $\boldsymbol{\delta}(\mathbf{k}) = FT(\Delta\phi/TE/\gamma\mu_0 H_0)$, can be represented as a weighted summation of susceptibility tensors as (6):

$$\boldsymbol{\delta}(\mathbf{k}) = a_{11}\boldsymbol{\chi}_{11}(\mathbf{k}) + a_{12}\boldsymbol{\chi}_{12}(\mathbf{k}) + a_{13}\boldsymbol{\chi}_{13}(\mathbf{k}) + a_{22}\boldsymbol{\chi}_{22}(\mathbf{k}) + a_{23}\boldsymbol{\chi}_{23}(\mathbf{k}) + a_{33}\boldsymbol{\chi}_{33}(\mathbf{k}) \quad [1]$$

where
$$a_{ij} = H_i H_i/3 - \mathbf{k}^{\mathrm{T}}\hat{\mathbf{H}}(k_i H_i)/k^2 \qquad (i = j)$$
$$a_{ij} = 2H_i H_j/3 - \mathbf{k}^{\mathrm{T}}\hat{\mathbf{H}}(k_i H_j + k_j H_i)/k^2 \qquad (i \neq j) \quad [2]$$

where $\hat{\mathbf{H}}$ is the direction of the applied field. Susceptibility tensor can be estimated by solving the following linear equations:

$$\boldsymbol{\delta} = \mathbf{A}\boldsymbol{\chi} \quad [3]$$

Since the main susceptibility contrast is determined by low spatial frequency component, while the imperfect image registration is characterized by high frequency errors, the following constraint was imposed at the peripheral k-space:

$$\boldsymbol{\chi}_{11}(\mathbf{k}) \approx \boldsymbol{\chi}_{22}(\mathbf{k}) \approx \boldsymbol{\chi}_{33}(\mathbf{k})$$
$$\boldsymbol{\chi}_{12}(\mathbf{k}) \approx \boldsymbol{\chi}_{13}(\mathbf{k}) \approx \boldsymbol{\chi}_{23}(\mathbf{k}) \quad [4]$$

This is implemented as a regularization term to Eq. 3 with a weighting function, $W(k)$, as:

$$W(k) = 1 - \left\{1 + \exp[(k-\alpha)/\beta]\right\}^{-1}, \quad [5]$$

$$\min \|\boldsymbol{\delta} - \mathbf{A}\boldsymbol{\chi}\| + W(k)\begin{pmatrix} \|\chi_{11}(k) - \chi_{22}(k)\| + \|\chi_{22}(k) - \chi_{33}(k)\| + \|\chi_{11}(k) - \chi_{33}(k)\| + \\ \|\chi_{12}(k) - \chi_{13}(k)\| + \|\chi_{13}(k) - \chi_{23}(k)\| + \|\chi_{12}(k) - \chi_{23}(k)\| \end{pmatrix} \quad [6]$$

According to Eq. 6, susceptibility tensor can be directly determined from the frequency shift exclusively.

RESULTS: The regularization parameters, α and β, were selected to match the degree of misregistration: the higher level of misregistration there is, the smaller α should be; β is adjusted to ensure a reasonably smooth transition to avoid any Gibbs ringing artifact. They were empirically set to $0.5k_{max}$ and $0.06k_{max}$, respectively. Fig. 1 shows the susceptibility tensors and mean susceptibility of human brain *in vivo* determined without and with regularization. The susceptibility tensors determined without regularization gives sharper tensors. However, a significant amount of variation in susceptibility tensor is observed at and near the gray and white matter interfaces, which differs significantly from the mean susceptibility map. These variations are most likely the errors associated with imperfect image registration. In contrast, the susceptibility tensors with regularization are slightly blurred, but the strong variations around the tissue interfaces are effectively eliminated. In addition, since the regularization assumes isotropic susceptibility for high-frequency component, it does NOT affect mean susceptibility calculation at all. The regularization also reduced erroneous patches in the vector field (Fig. 1. right column). Fig. 2 shows the eigenvectors and the fiber tracking of anterior commissue in mouse brain *ex vivo*. Since the image distortion in the mouse brain is less comparing with human brain and the image registration can be done much better, the anterior commissure fiber tracks determined without and with regularization is very similar (Fig. 2), except in certain regions (green arrow) the regularized method gives slightly more fiber than that without regularization.

CONCLUSION: The regularized k-space-based method improves the robustness of STI by reducing the artifact associated imperfect image registration at the cost of slightly blurred tensor maps. This regularization approach does not affect the calculation of mean susceptibility. In summary, this method is useful for enhancing the robustness of in vivo application of STI of human brain and the application of STI-based fiber tracking in ex vivo mouse brain.

REFERENCES: (1) He and Yablonskiy PNAS 2009. (2) Lee et al, PNAS, 2010. (3) Wiggins et al., Proc ISMRM, 2008; (4) Schäfer et al., Proc ISMRM, 2009. (5) Liu, MRM 2009. (6) Liu et al, NeuroImage, 2011. (7) Li et al, NeuroImage 2011, (8) Schweser et al, NeuroImage, 2011.

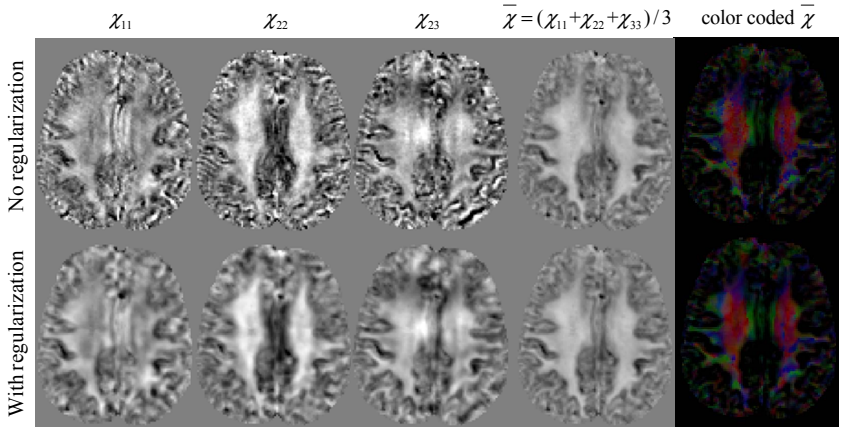

Fig. 1. STI of human brain *in vivo* without and with regularization.

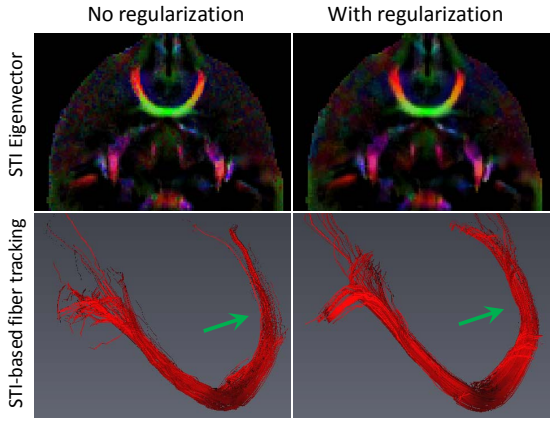

Fig.2 STI-based fiber tracking in mouse brain *ex vivo*