Diffusion-Relaxation Correlation Spectroscopic Imaging (DR-CSI): An Enhanced Approach to Imaging Microstructure

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Synopsis

We propose a new MR experiment called diffusion-relaxation correlation spectroscopic imaging (DR-CSI). DR-CSI acquires imaging data across a range of different b-value and echo time combinations, and then performs regularized reconstruction to generate a 2D diffusion-relaxation correlation spectrum for every voxel. The peaks of this spectrum correspond to the different tissue microenvironments that are present within each macroscopic imaging voxel, which provides powerful insight into the tissue microstructure. Compared to standard relaxometry or diffusion imaging, DR-CSI provides unique capabilities to resolve tissue compartments that have similar relaxation or diffusion parameters. DR-CSI is demonstrated with spinal cord traumatic injury MRI data.

Purpose

MR relaxometry and diffusion imaging have each been proposed as methods that can probe microscopic tissue compartments using standard millimeter-scale spatial resolution. For example, relaxometry can be used to estimate the amount of myelin content within a voxel [1,2], while diffusion imaging can be used to quantify the neurite density, the size of the extracellular space, and the presence of edema [3-5]. However, both of these modalities are subject to ambiguities and confounds whenever the diffusion or relaxation parameters of two distinct tissue microenvironments are too similar to one another.

Diffusion-relaxation correlation spectroscopy (DR-COSY) is a (single-voxel, non-imaging) 2D spectroscopic method that encodes diffusion and relaxation parameters jointly, and substantially improves the ability to distinguish different tissue compartments [6-9]. This work proposes and evaluates a novel imaging extension of DR-COSY, which we name diffusion-relaxation correlation spectroscopic imaging (DR-CSI). Enabled by regularization strategies that help to overcome the ill-posedness of the problem, DR-CSI provides a 2D spectrum of information for every voxel. The peaks of this 2D spectrum can be integrated and displayed as spatial maps of the different tissue microcompartments as they vary across the field-of-view. The potential usefulness of DR-CSI is illustrated using ex vivo mouse spinal cord traumatic injury data.

Methods

Diffusion-relaxation data acquisition: We acquired 28 different simultaneously diffusion- and relaxation-encoded images. Specifically, we acquired 7 different b-values (b = 0, 500, 1000, 2000, 3000, 4000 and 5000 s/mm2), and measured data at 4 different echo times for each b-value (TE = 40, 80, 120 and 160 ms). We acquired six ex vivo mice spinal cord data sets (three sham controls and three with traumatic spinal cord injury as described in [10]).

Diffusion-T2 correlation spectral analysis: We modeled the measured DR-CSI signal as a mixture of 2D exponential decays:

$$M(x,y,b,TE) = \int\int F(x,y,D,T_2)\, e^{-bD} e^{-\frac{TE}{T_2}}\, dD\, dT_2,$$

where $M(x,y,b,TE)$ is the measured data at spatial position (x,y), diffusion encoding b, and echo time TE, and $F(x,y,D,T_2)$ is the spatially-varying diffusion-relaxation correlation spectrum as a function of the diffusion coefficient D and relaxation parameter T_2. Conventionally, 2D inverse Laplace transforms have been used to estimate 2D DR-COSY spectra [11]. However, these approaches typically require a larger number of diffusion-relaxation encodings and higher SNR, which is only practical with the large voxel sizes that are common in spectroscopic applications. To enable DR-CSI with a smaller number of encodings and lower SNR, we performed regularized 2D spectrum estimation using the prior information that $F(x,y,D,T_2)$ is nonnegative and will exhibit smooth spatial variation. Based on these assumptions, $F(x,y,D,T_2)$ was estimated by solving a dictionary-based spatially-regularized nonnegative least squares optimization problem. To reduce computational complexity for this high-dimensional optimization problem, we designed an efficient reconstruction algorithm based on variable splitting and the alternating direction method of multipliers [12].

Results

Figure 1 shows spatially-averaged DR-CSI spectra for control and injured spinal cords. The control spectrum has two distinct well-resolved peaks, as well as a third weaker peak in between. In contrast, the spectrum for the injured cord contains an additional peak that was not present in the control

spectrum. Importantly, these distinct peaks are only well-resolved in the 2D spectra, while there is considerable ambiguity in the 1D diffusion-only and relaxation-only spectra which resolve substantially fewer peaks.

Figure 2 shows spatial maps of the integrated spectral peaks from Fig. 1. This figure shows that the estimated peaks from Fig. 1 seem to correspond to tissue microenvironments that are consistent with the known anatomy of the spinal cord. Specifically, one of the peaks appears to correspond to white matter (WM), one appears to correspond to ventral gray matter (VGM), one appears to be present in both the dorsal gray matter and the white matter to a lesser degree (DGM), and one seems specific to the injured cords (injury). It should be noted that these spatial maps have considerable spatial overlap, demonstrating that DR-CSI can successfully disentangle partial volume contributions from multiple tissue compartments within the same voxel. This is illustrated even further in Fig. 3, which shows spatially-varying spectra from the WM-GM boundary, as the tissue transitions between WM and VGM.

Discussion and Conclusion

We have proposed a novel approach to imaging tissue microstructure with enhanced capabilities for identifying distinct tissue microcompartments, and have demonstrated its potential in both healthy and injured tissues. We expect the DR-CSI technique substantially expand the usefulness of MR relaxometry and diffusion imaging for studies of tissue microstructure.

Acknowledgements

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References

[1] A. MacKay, C. Laule, I. Vavasour, T. Bjarnason, S. Kolind, B. Madler. “Insights into brain microstructure from the T2 distribution.” Magn. Reson. Imaging, vol. 24(4), pp. 515-525, 2006.

[2] S. C. Deoni. "Quantitative relaxometry of the brain." Top. Magn. Reson. Imaging, vol. 21(2), pp. 101-113, 2010.

[3] H. Zhang, T. Schneider, C. A. Wheeler-Kingshott, D. C. Alexander. “NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain.” Neuroimage, vol. 61(4), pp. 1000-1016, 2012.

[4] Y. Assaf, R. Z. Freidlin, G. K. Rohde, P. J. Basser. “New modeling and experimental framework to characterize hindered and restricted water diffusion in brain white matter.” Magn. Reson. Med., vol. 52(5), pp. 965–978, 2004.

[5] Y. Wang, Q. Wang, J. P. Haldar, F.-C. Yeh, M. Xie, P. Sun, T.-W. Tu, K. Trinkaus, R. S. Klein, A. H. Cross, S.-K. Song. “Quantification of increased cellularity during inflammatory demyelination.” Brain, vol. 134, pp. 3587-3598, 2011.

[6] M.D. Hurlimann, L. Venkataramanan, C. Flaum. “The diffusion-spin relaxation time distribution function as an experimental probe to characterize fluid mixtures in porous media.” J. Chem. Phys., vol. 117, pp. 10223-10232, 2002.

[7] P. T. Callaghan, S. Godefroy, B. N. Ryland. “Use of the second dimension in PGSE NMR studies of porous media.” Magn. Reson. Imaging, vol. 21(3-4), pp. 243-248, 2003.

[8] B. Dhital, M. Gratz, and R. Turner. “Diffusion relaxation correlation spectroscopy at ultra short echo times reveals two major compartments in human cadaver brain white matter.” ISMRM 2011, 3944

[9] H. Celik, Mu. Bouhrara, D. A. Reiter, K. W. Fishbein, R. G. Spencer. “Stabilization of the inverse Laplace transform of multiexponential decay through introduction of a second dimension.” J. Magn. Reson., vol. 236, pp. 134-139, 2013.

[10] J. H. Kim, T.-W. Tu, P. V. Bayly, S.-K. Song. “Impact speed does not determine severity of spinal cord injury in mice with fixed impact displacement.” J. Neurotrauma, vol. 26(8), pp. 1395-1404, 2009.

[11] Y.-Q. Song, L. Venkataramanan, M. D. Hürlimann, M. Flaum, P. Frulla, C. Straley. “correlation spectra obtained using a fast two-dimensional Laplace inversion.” J. Magn. Reson., vol. 154(2), pp. 261–268, 2002.

[12] M. V. Afonso, J. M. Bioucas-Dias, M. A. T. Figueiredo. “Fast image recovery using variable splitting and constrained optimization.” IEEE Trans. Image Process., vol. 19(9), pp. 2345-2356, 2010.

Figures

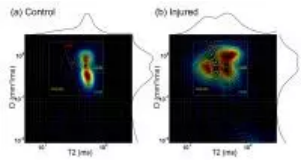

Fig.1. DR-CSI-based 2D spectra obtained from (a) control and (b) injured spinal cords, averaged across all voxels. We also show projected 1D relaxation-only spectra and 1D diffusion-only spectra along the top and right sides of each 2D spectrum. Importantly each 2D spectrum resolves more distinct peaks (corresponding to distinct tissue microenvironments) than are resolved in the 1D spectra.

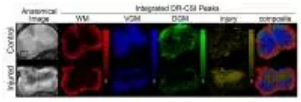

Fig.2. Spatial maps of the integrated spectral peaks from the DR-CSI reconstruction of (top) control and (bottom) injured spinal cords. The spectral regions that were integrated to obtain each spatial map are indicated in the 2D diffusion-relation correlation spectra from Fig. 1.

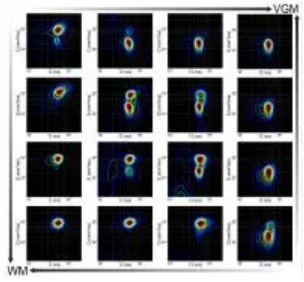

Fig.3. Spatially-varying DR-CSI spectra from the boundary between WM and VGM in the control cord, corresponding to the black box drawn on the anatomical image in Fig. 2. DR-CSI successfully disentangles partial volume effects in the transition region between the two tissues.