High-Resolution Brain Metabolite T2 Mapping Using Optimized Multi-TE MRSI

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Synopsis

Metabolite T2 is recognized as an important physiological and disease biomarker, whose measurement also benefits metabolite quantification. However, the SNR challenge of MRSI and prolonged scan time for multi-TE acquisition limit the imaging resolution. This work presents an optimized multi-TE MRSI strategy to achieve high-resolution 3D brain metabolite T2 mapping. Specifically, estimation-theoretic TE selection was analyzed for optimized metabolite T2 estimation. An enhanced parameter estimation strategy was proposed. Both simulation and invivo studies were conducted to evaluate our method. The exciting capability of simultaneous high-resolution metabolite, neurotransmitter and T2 mapping is demonstrated for the first time.

Introduction

The relaxation parameters of brain metabolites, e.g., T2, are important physiological and disease biomarkers [1-4]. Estimation of molecule-specific T2 can also be beneficial for metabolite quantification.[5-6] However, due to the inherent SNR challenge of MRSI and prolonged scan time for acquiring data at multiple TEs to encode the T2 decays, existing metabolite T2 estimation studies are restricted to single voxels or low-resolution 2D acquisitions (around 1 cm^3 voxels)[2-9]. In this work, we present a novel method that synergizes recent developments in rapid, high-resolution MRSI acquisition[10,11], estimation-theoretic optimization of nonuniform TE selection, and subspace-based reconstruction and quantification, to enable high-resolution mapping of brain metabolite T2. Theoretical analysis, simulations, and experimental studies were performed to evaluate the effectiveness of optimized TE selection in improving the T2 estimation and our processing methods in achieving high-resolution brain metabolite T2 mapping. The capability of simultaneous 3D metabolite, neurotransmitter, and T2 mapping is demonstrated for the first time.

Theory and Methods

<u>Optimized experiments for multimolecular T2 estimation:</u>

It has been shown that uniform, many-TE acquisitions are suboptimal for metabolite quantification in multi-TE MRSI[10,12,13], while investigation on optimal MRSI experimental design for T2 mapping is scarce. We developed a Cramer-Rao bound (CRB) analysis to optimize MRSI acquisitions for T2 mapping. We consider the following signal model with an explicit representation of metabolite T2[14]:

$$s_{TE}[m] = e^{i\varphi_0}\left(\sum_{n=1}^{N} c_n \phi_{n,TE}(m\Delta t) e^{-[TE+m\Delta t]/T_{2,n}} e^{\left(-[m\Delta t]/T'_{2,n}\right)} e^{\left(-[m\Delta t]^2 g\right)}\right) + \xi_{TE}[m], (1)$$

where $s_{TE}[m]$ and $\xi_{TE}[m]$ represent the TE-dependent FIDs and noise, Δt denotes sampling interval with m the index, $\phi_{n,TE}$ the TE-dependent metabolite basis, c_n the concentrations, $T_{2,n}$ and $T'_{2,n}$ the relaxation and lineshape parameters, φ_0 a global zeroth-order phase and g captures the Gaussian lineshape. Using Eq(1), the TE-number and TE-value-dependent Fisher Information Matrix (FIM) for all the unknown parameters $\boldsymbol{\theta} = \left[c_1, \ldots c_N, T_{2,1}, \ldots, T_{2,n}, T'_{2,1}, \ldots, T'_{2,n}, \varphi_0, g\right]^T$ can be calculated[15](details omitted). The CRB of target parameters can be computed from inverse FIM and minimized. With this flexibility, we chose here to minimize the T2 estimation variances for NAA, Cr, and Cho. Specifically, we minimize CRB under **an equivalent-time** constraint for fair comparisons. Since fitting T2 from single TE is extremely ill-conditioned, we performed the CRB calculation from 2 to 12 TEs (exhausted combinatorial search for the first 2 optimal TEs and greedy search for additional TEs). This allowed us to identify an optimized 4-TE combination (Fig.1).

<u>Spatiospectral reconstruction and parameter estimation:</u>

The fast sequence described in [11] is used to acquire data at selected TEs. Nuisance removal was performed using a multi-TE adapted union-of-subspaces (UoSS) model[11,16]. A subspace constrained reconstruction was done using a learned multi-TE metabolite subspace to generate TE-dependent spatiospectral functions[11,17].

An enhanced multi-TE subspace approach is proposed to improve the parameter estimation, inspired by [18]. Specifically, a targeted multi-TE UoSS fitting was applied to separate different molecular components of interest from the reconstruction[12], e.g.,

$$\hat{\rho}(\mathbf{r}, t_1, t_2) = \sum_{l_{NAA}=1}^{L_{NAA}} c_{l_{NAA}}(\mathbf{r}) v_{l_{NAA}}(t_1, t_2) + \sum_{l_{Cr}=1}^{l_{Cr}} c_{l_{Cr}}(\mathbf{r}) v_{l_{Cr}}(t_1, t_2) + \sum_{l_{Cho}=1}^{L_{Cho}} c_{l_{Cho}}(\mathbf{r}) v_{l_{Cho}}(t_1, t_2) + \sum_{l_{other}=1}^{L_{other}} c_{other}(\mathbf{r}) v_{other}(t_1, t_2), (2)$$

where t_2 and t_1 denote the chemical shift and TE dimensions, respectively. The multi-TE basis $\{v_{l_x}(t_2, t_1)\}$ with component-specific orders l_x are learned subspaces with lineshape-adapted to $\hat{\rho}(\mathbf{r}, t_1, t_2)$. Spatial constraints were used during a regularized least-squares fitting of the coefficients in Eq(2). Task-specific parameter can then be estimated by parametric fitting (e.g.,ProFit[14]) of the separated components.

Results

The computational multi-TE MRSI phantom in [12] was extended to include T2 spatial variations for Monte-Carlo analysis of our TE optimization and estimation strategies. In vivo data were acquired on a 3T Prisma (IRB approved) with TE-dependent (k_y,k_z)-undersampling to extend the k-space coverage. The total acquisition time is ~ 24 mins for 4 TEs at a 3.4×3.4×6.4 mm^3 nominal resolution. An equivalent-time scan with literature TEs was also performed for comparison. Figure 1 shows the T2 CRBs of NAA, Cr, Cho, and their combination (denoted as brain metabolite) for all 2-TE combinations and more TE numbers. The brain metabolite CRB is driven by the component with higher variances (i.e, Cr and Cho) and reaches the minimum (~17ms)

at 4 TEs while acquiring more TEs is not necessarily reducing estimation variance. The standard deviation maps from Monte-Carlo simulations clearly demonstrate the reduced variance achieved by our optimized 4-TE selection compared to literature 4 TEs (Fig.2), both from the same parametric fitting. Moreover, the proposed strategy further improves the estimation with the same TE selection. High-resolution 3D in vivo T2 maps for NAA, Cr, and Cho were produced using our optimized 4-TE acquisition and processing strategies (Fig.3). White/gray matter contrast in NAA T2 map can be observed, consistent with prior data. Reduced estimation variance for all metabolites can be seen for the optimized acquisition using a regional analysis (Fig.4). Results from the non-optimized TE set yielded over-estimated T2 of Cho and larger variances. The capability of simultaneously mapping metabolites, neurotransmitters, and T2s is demonstrated in Fig.5. These results suggest the task-specific optimization flexibility of the proposed method.

Conclusion

A new method is proposed to achieve high-resolution brain metabolite T2 mapping. Estimation-theoretic analysis, simulations and experimental studies validate the proposed method and support the exciting capabilities of simultaneously 3D mapping of brain metabolites and their T2 parameters.

Acknowledgements

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Figures

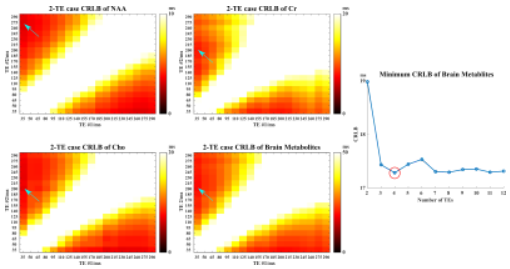

Figure 1: CRB analysis for brain metabolite T2 estimation. Column 1 and 2 show the CRB maps of 2-TE combinations for NAA, Cr, and Cho (their combination referred to as brain metabolites). The optimal 2-TE choice (lowest CRB) is marked by the blue arrow. Column 3 shows the minimum CRB of brain metabolites w.r.t. the number of TEs under equivalent time comparison (repeat selections allowed). The minimal CRLB is achieved at 4 TEs, which is selected for further analysis.

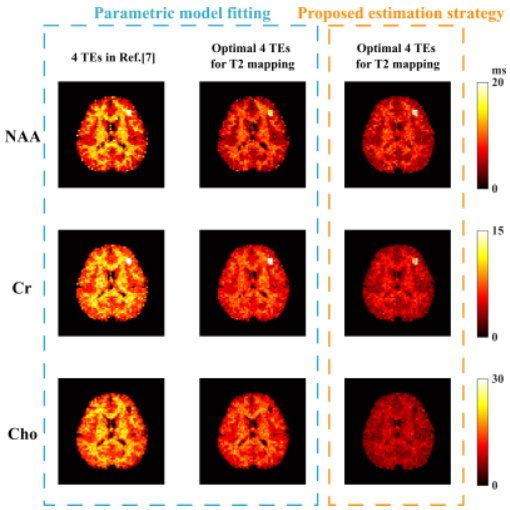

Figure 2: Standard deviation (std) maps (unit in ms) for NAA, Cr, and Cho T2 estimates (row 1-3) from Monte-Carlo analysis. The first two columns compare different 4-TE combinations using the same parametric fitting. Significantly reduced estimation variance was achieved by TE optimization (Col. 2: [35, 200, 245, 275] ms) compared to a literature choice[7] (Col. 1: [50, 100, 160, 220] ms), which is consistent with CRB analysis. Our estimation strategy further reduced the estimation variances with the optimized TEs, demonstrating its effectiveness.

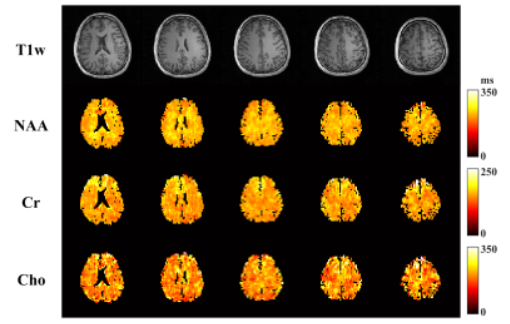

Figure 3: High-resolution 3D brain metabolite T2 maps from in vivo MRSI data (3.4×3.4×6.4 mm^3 nominal voxels) acquired at the optimized 4 TEs. Anatomical images (T1w) across different slices are shown in the first row. T2 maps for NAA, Cr, and Cho estimated using the proposed method are shown in subsequent rows excluding CSF-dominant voxels (low concentrations not reliable for T2 fitting). White/gray matter contrast can be visualized in NAA T2 maps and less contrast for Cr T2 maps, consistent with previous findings.

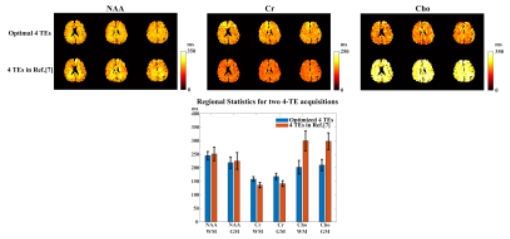

Figure 4: Comparison of acquisitions using optimized 4 TEs and literature TEs, with regional statistical analysis. Metabolite T2 maps are shown in the top panel (row 1 being the results from optimized 4 TEs) and regional analysis in the bottom. Reduced estimation variance from optimized 4-TE data can be

observed for all 3 metabolites, consistent with CRB analysis and MC simulations. Regional T2's from our method are consistent with literature values[7,9]. The optimized acquisition and estimation mitigate the over-estimation of Cho T2, apparent in both the maps and regional values.

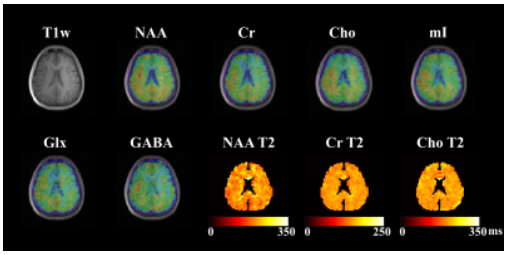

Figure 5: Metabolite, neurotransmitter, and metabolite T2 maps generated from a single 4-TE scan (healthy volunteer). The first 2 TEs were optimized for Glx and GABA estimation, and the remaining 2 TEs were selected by greedy searching the minimal CRB for T2s of NAA, Cr, and Cho. One slice from the 3D volume was chosen to showcase the multiplexed molecular mapping capability, demonstrating the rich biological information that can be provided by multidimensional, multiparametric MRSI.