Optimizing MR Scan Design for Parameter Estimation (with Application to T_1, T_2 Relaxometry)

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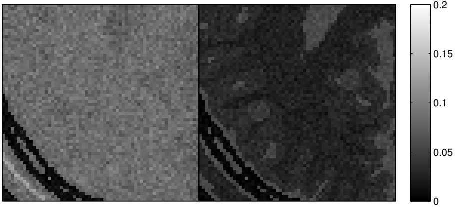
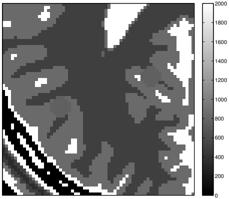
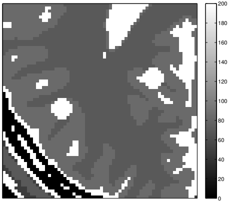
Why Quantitative MRI?



(a) Anatomical Image



(b) Latent T_1 Map



(c) Latent T_2 Map

Anatomical vs. Quantitative MR Imaging (QMRI)

Anatomical MRI: seek to reconstruct *qualitative* images

- ✓ *Linearly* related via Fourier transform to raw **k**-space data
- ✗ Same anatomy + varied acquisitions = varied image contrasts!
- ✗ Confounds *nuisance* contrast mechanisms with those *of interest*

Quantitative MRI: seek to estimate *intrinsic* parameters of interest

- ✓ Parameter maps are **physical** and have **direct medical relevance**
- ✓ Tissue alterations detectable with **high sensitivity**
- ✓ Many studies suggest (potential) clinical applications
  - Brain: multiple sclerosis, epilepsy, Parkinson's, ...
  - Other: cartilage degeneration, cardiac edema/infarction, ...
- ✗ In general, *nonlinearly* related to **k**-space data → challenging recon
- ✗ Well-conditioned estimation typically requires careful **scan repetition** with varied scan parameters → **increased acquisition time**

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How to popularize QMRI clinically?

Multidisciplinary approaches:

- **Health sciences**: find specific applications for which QMRI outperforms as a diagnostic or prognostic tool (Cheng et al., 2012)
- **Hardware engineering**: improve MR hardware to produce better data (higher SNR, better field uniformity, etc.) (Roemer et al., 1990)
- **Image reconstruction**: for a given dataset, estimate latent parameters of interest rapidly and "reliably" (Nataraj et al., 2014)
- **Data acquisition**: prescribe a fast *scan profile*, or a combination of scan parameters from one or more pulse sequences, that enables "good" parameter estimation
  - Prior work: measured with CNR variations (Deoni et al., 2003, 2004)
  - This talk: measured with estimator **precision** (Nataraj et al., 2015)

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Problem Statement

We seek a systematic method to guide **robust scan design** to enable **precise** latent object parameter estimation.

Scan design consists of two subproblems:

1. *Scan profile selection*
   Given a collection of candidate pulse sequences, how to best assemble a scan profile?
2. *Scan parameter optimization*
   For a fixed time constraint, how to optimize a given scan profile's acquisition parameters for latent object parameter estimation?

Robust means unbiased estimators maintain high precision across a wide range of object parameters

General signal model

Many MR pulse sequences yield images (at position $\mathbf{r}$) described as:

$$y_d(\mathbf{r}) = f_d(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{p}_d) + \epsilon_d(\mathbf{r}), \; d = 1, \dots, D \tag{1}$$

Notation:

- $\mathbf{x}(\mathbf{r}) \in \mathbb{C}^L$ collects L *latent* object parameters at $\mathbf{r}$
- $\boldsymbol{\nu}(\mathbf{r}) \in \mathbb{C}^K$ collects K *known* object parameters at $\mathbf{r}$
- $\mathbf{p}_d \in \mathbb{R}^P$ denotes set of P scan parameters for dth dataset
- $\epsilon_d(\mathbf{r}) \sim \mathbb{C}\mathcal{N}(0, \sigma_d^2)$ modeled as independent, complex Gaussian noise[1]

[1] Here, $\mathbf{k}$-space taken as fully-sampled on Cartesian grid

Scan profile model

A candidate scan profile collects D datasets from a combination of (possibly different) pulse sequences:

$$\mathbf{y}(\mathbf{r}) = \mathbf{f}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P}) + \boldsymbol{\epsilon}(\mathbf{r}) \tag{2}$$

Notation:

- $\mathbf{y}(\mathbf{r}) := [y_1(\mathbf{r}), \ \ldots, \ y_D(\mathbf{r})]^\mathsf{T} \ \in \ \mathbb{C}^D$ collects noisy signals
- $\mathbf{f} : \mathbb{C}^L \times \mathbb{C}^K \times \mathbb{R}^{P \times D} \mapsto \mathbb{C}^D$ naturally extends scalar function f
- $\mathbf{P} := [\mathbf{p}_1, \ \ldots, \ \mathbf{p}_D] \in \mathbb{R}^{P \times D}$ gathers all scan parameters
- $\boldsymbol{\epsilon} \in \mathbb{C}^D$ denotes Gaussian noise with diagonal covariance matrix $\boldsymbol{\Sigma}$

The Cramér-Rao Bound

Log-likelihood function (to within a constant c):

$$\ln L(\mathbf{x}(\mathbf{r})) = -\frac{1}{2}\left\|\mathbf{y}(\mathbf{r}) - \mathbf{f}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P})\right\|^2_{\boldsymbol{\Sigma}^{-1/2}} + c \tag{3}$$

Fisher information matrix: useful for characterizing estimator precision:

$$\begin{aligned} \mathbf{F}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P}) &:= \mathbb{E}\left([\nabla_{\mathbf{x}} \ln L(\mathbf{x}(\mathbf{r}))]^\dagger \, [\nabla_{\mathbf{x}} \ln L(\mathbf{x}(\mathbf{r}))] \right) \\ &= [\nabla_{\mathbf{x}} \mathbf{f}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P})]^\dagger \, \boldsymbol{\Sigma}^{-1} \, [\nabla_{\mathbf{x}} \mathbf{f}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P})] \end{aligned} \tag{4}$$

(Matrix) Cramér-Rao Bound on covariance of unbiased estimates:

$$\operatorname{cov}\left(\widehat{\mathbf{x}}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P}\right) \succeq \mathbf{F}^{-1}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P}) \tag{5}$$

Towards an Objective Function

Desirable to choose $\mathbf{P}$ such that precision matrix $\mathbf{F}^{-1}$ "small"

Statisticians have considered minimizing various summary statistics:

- *G*-optimality: $\max \operatorname{diag}\left(\mathbf{F}^{-1}\right)$ (Smith, 1918)
- *D*-optimality: $\det\left(\mathbf{F}^{-1}\right)$ (Wald, 1945)
- *A*-optimality: $\operatorname{tr}\left(\mathbf{F}^{-1}\right)$ (Chernoff, 1953)
- ...

We consider a weighted variation of *A*-optimality:

$$\Psi(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P}) = \operatorname{tr}\left(\mathbf{W}\mathbf{F}^{-1}(\mathbf{x}(\mathbf{r}); \boldsymbol{\nu}(\mathbf{r}), \mathbf{P})\mathbf{W}^{\top}\right) \tag{6}$$

- Diagonal weight matrix $\mathbf{W} \in \mathbb{R}^{L \times L}$ controls relative importance of precisely estimating L latent object parameters

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Min-max Optimization

Cannot minimize $\Psi(\mathbf{x}; \boldsymbol{\nu}, \mathbf{P})$ directly due to spatial variation of $\mathbf{x}(\cdot)$ and $\boldsymbol{\nu}(\cdot)$

Instead, seek candidate scan parameters $\check{\mathbf{P}}$ that *minimize* the *max* cost $\widetilde{\Psi}^{\mathrm{t}}$:

$$\check{\mathbf{P}} \in \arg\min_{\mathbf{P} \in \mathcal{P}} \widetilde{\Psi}^{\mathrm{t}}(\mathbf{P}), \qquad \text{where} \tag{7}$$

$$\widetilde{\Psi}^{\mathrm{t}}(\mathbf{P}) = \max_{\substack{\mathbf{x} \in \mathcal{X}_{\mathrm{t}} \\ \boldsymbol{\nu} \in \mathcal{N}_{\mathrm{t}}}} \Psi(\mathbf{x}; \boldsymbol{\nu}, \mathbf{P}). \tag{8}$$

More notation:

- Search space $\mathcal{P}$ can incorporate scan time constraints
- *Tight* latent object parameter set $\mathcal{X}_{\mathrm{t}}$ chosen based on **application**
- *Tight* known object parameter set $\mathcal{N}_{\mathrm{t}}$ chosen using **prior knowledge**

Incorporating Robustness

Generally, $\Psi(\mathbf{x}; \boldsymbol{\nu}, \mathbf{P})$ is non-convex, and may have multiple global minimizers and/or near-global minimizers. Collect these candidates as

$$\mathcal{S} := \left\{ \mathbf{P} : \widetilde{\Psi}^{\mathrm{t}}(\mathbf{P}) - \widetilde{\Psi}^{\mathrm{t}}(\check{\mathbf{P}}) \leq \delta \widetilde{\Psi}^{\mathrm{t}}(\check{\mathbf{P}}) \right\}, \qquad \text{where } \delta \ll 1. \tag{9}$$

Robustness problem – select *one* scan parameter $\mathbf{P}^*$ that degrades least when worst-case cost viewed over *broadened* sets $\mathcal{X}_{\mathrm{b}}$ and $\mathcal{N}_{\mathrm{b}}$:

$$\mathbf{P}^* = \arg\min_{\mathbf{P} \in \mathcal{S}} \widetilde{\Psi}^{\mathrm{b}}(\mathbf{P}), \qquad \text{where} \tag{10}$$

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Summary: *Robust, Application-specific* Scan Design

Recall: We sought a systematic method to guide **robust scan parameter optimization** *and* **scan profile selection**

- ✓ Candidate scan parameters $\mathcal{S}$ found via min-max problem (7)
- ✓ Robust parameter $\mathbf{P}^*$ chosen from $\mathcal{S}$ via robustness problem (10)
- ✗ Scan profile selection?...
  - Given some candidate pulse sequences, construct all possible scan profiles that satisfy constraints, *e.g.*, acquisition time
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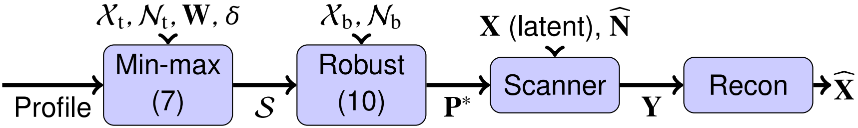
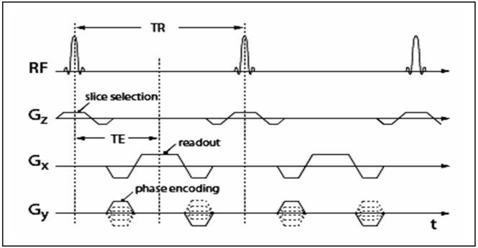


MR Parameters of Interest



Prescribed scan parameters, $\mathbf{p}$

- T_R: repetition time between RF excitations
- a_0: nominal flip angle by which spins are tipped

Latent object parameters, $\mathbf{x}(\mathbf{r})$

- $T_1(\mathbf{r}), T_2(\mathbf{r})$: longitudinal and transverse relaxation times (**of interest**)
- $M_E(\mathbf{r})$: spin density (**nuisance**)

Known object parameters, $\boldsymbol{\nu}(\mathbf{r})$

- $\kappa(\mathbf{r})$: spatial variation in flip angle (true flip is $a_0\kappa(\mathbf{r})$)

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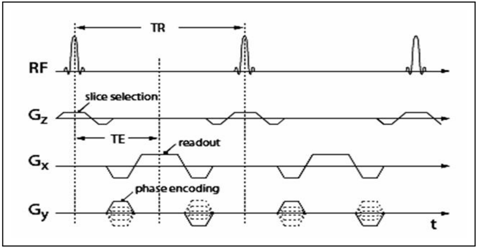

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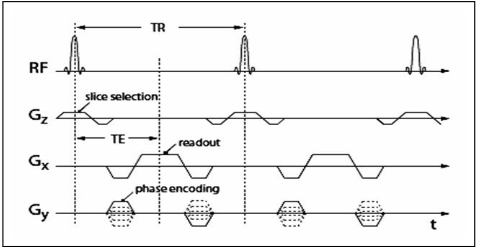

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Detailed Application

Example Problem: scan design for joint T_1, T_2 estimation in brain

1. Candidate (fast) pulse sequences
   - **Spoiled Gradient-Recalled Echo (SPGR)**: sensitive to T_1
   - **Dual-Echo Steady-State (DESS)**: sensitive to T_1, T_2
2. Candidate scan profiles
   - Profile consisting of C_{SPGR} SPGR and C_{DESS} DESS scans yields $D = C_{\text{SPGR}} + 2C_{\text{DESS}}$ datasets
   - Can write SPGR, DESS signal models to group $L = 3$ latent object parameters $\mathbf{x}(\mathbf{r}) := [M_{\text{E}}(\mathbf{r}), T_1(\mathbf{r}), T_2(\mathbf{r})]^{\mathsf{T}}$ together
   - Prior works have considered T_1 and T_2 estimation from as few as 2 SPGR (Deoni et al., 2003) or 1 DESS (Welsch et al., 2009) scan(s)
   - Examine scan profiles no longer than $(C_{\text{SPGR}}, C_{\text{DESS}}) = (\mathbf{2}, \mathbf{1})$ profile
   - Ensuring $D \geq L = 3$, only other possibilities: $(\mathbf{1}, \mathbf{1})$ and $(\mathbf{0}, \mathbf{2})$
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Scan Profile Comparisons: Visualization

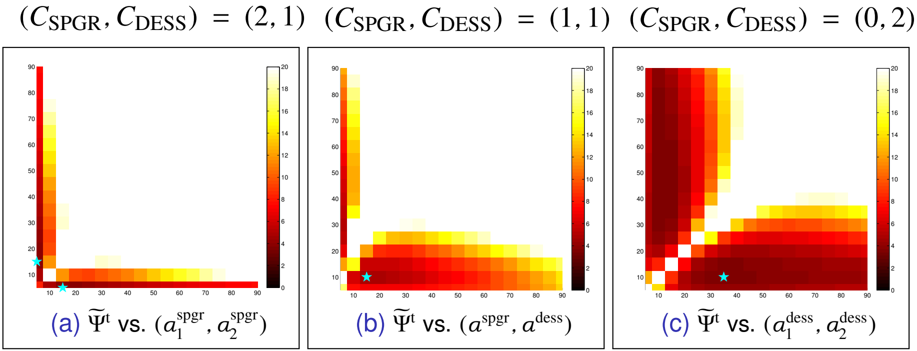

Figure 1: Appears that $\widetilde{\Psi}^{\text{t}}$ at minimizers are similar, but the optimized $(0, 2)$ profile appears most robust to flip angle variation. All values in milliseconds.

Scan Profile Comparisons: Performance Summary

Scan	$\widehat{a}_0^{\text{spgr}}$	$\widehat{a}_0^{\text{dess}}$	$\widehat{T}_R^{\text{spgr}}$	$\widehat{T}_R^{\text{dess}}$	$\widetilde{\Psi}^{\text{t}}(\mathbf{P}^*)$	$\widetilde{\Psi}^{\text{b}}(\mathbf{P}^*)$
$(2, 1)$	(15, 5)°	30°	(12.2, 12.2)	17.5	4.0	17.7
$(1, 1)$	15°	10°	13.9	28.0	4.9	17.9
$(0, 2)$	–	(35, 10)°	–	(24.4, 17.5)	**3.5**	**12.2**

Table 1: Reflecting Fig. 1, $\widetilde{\Psi}^{\text{b}}$ recommends $(0, 2)$ more emphatically than $\widetilde{\Psi}^{\text{t}}$. Flip angles are in degrees; all other values are in milliseconds.

New findings:

- DESS sequences alone can be useful for precise T_1 mapping
- For certain applications (not shown), better to increase acquisition time for each existing scan, rather than collecting an additional scan

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Simple simulation study

Neglect to model several effects to simplify study of estimator statistics:

- No transmit field inhomogeneity
- No receive coil sensitivity variation
- No partial volume effects: deterministic knowledge of WM/GM ROIs
- ...

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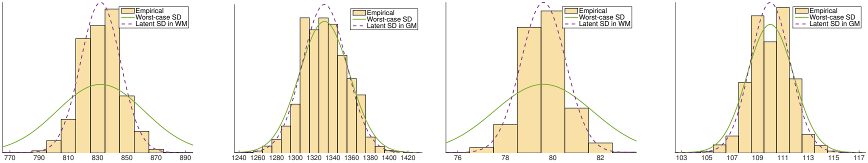
Estimator statistics



(a) $\widehat{T}_1^{\mathrm{ML}}$ in WM voxels (ms)

(b) $\widehat{T}_1^{\mathrm{ML}}$ in GM voxels (ms)

(c) $\widehat{T}_2^{\mathrm{ML}}$ in WM voxels (ms)

(d) $\widehat{T}_2^{\mathrm{ML}}$ in GM voxels (ms)

Figure 2: At realistic noise levels, ML estimates exhibit negligible bias and appear nearly Gaussian-distributed. Thus, CRB reliably approximates $\widehat{T}_1^{\mathrm{ML}}, \widehat{T}_2^{\mathrm{ML}}$ errors.

(Selected) Acquisition/Reconstruction Details

Fast steady-state acquisitions

- Combinations of $(2, 1)$, $(1, 1)$, and $(0, 2)$ SPGR and DESS scans
- Prescribe flip angles $\widehat{\boldsymbol{a}}$ and repetition times $\widehat{\mathbf{T}}_{\mathrm{R}}$ in Table 1
- $256 \times 256 \times 6$ matrix over $240 \times 240 \times 30$mm FOV
- Effective scan time: **10.73s** per slice

Slow reference acquisitions

- Optimized combination of 2 IR scans for reference $\widehat{T_1}$ map
- Optimized combination of 2 SE scans for reference $\widehat{T_2}$ map
- 256×256 matrix over $24 \times 24 \times 5$mm FOV
- Effective total scan time: **51m12s** per slice

Reconstruction overview

- Regularized Least Squares (RLS) optimization using ML initialization, followed by alternating minimization
- Flip angle variation $\widehat{\kappa}(\mathbf{r})$ separately estimated from pair of Bloch-Siegert (BS) shifted SPGR scans

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Fast steady-state acquisitions

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- Prescribe flip angles $\widehat{\boldsymbol{a}}$ and repetition times $\widehat{\mathbf{T}}_{\mathrm{R}}$ in Table 1
- $256 \times 256 \times 6$ matrix over $240 \times 240 \times 30$mm FOV
- Effective scan time: **10.73s** per slice

Slow reference acquisitions

- Optimized combination of 2 IR scans for reference $\widehat{T}_1$ map
- Optimized combination of 2 SE scans for reference $\widehat{T}_2$ map
- 256×256 matrix over $24 \times 24 \times 5$mm FOV
- Effective total scan time: **51m12s** per slice

Reconstruction overview

- Regularized Least Squares (RLS) optimization using ML initialization, followed by alternating minimization
- Flip angle variation $\widehat{\kappa}(\mathbf{r})$ separately estimated from pair of Bloch-Siegert (BS) shifted SPGR scans

(Selected) Acquisition/Reconstruction Details

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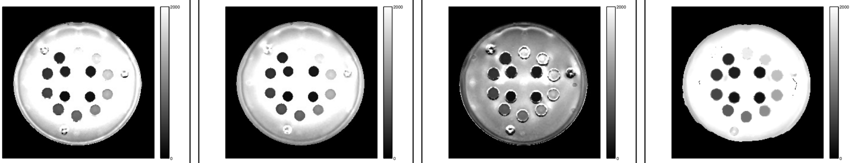
Phantom Results: T_1

Coronal scans of **NIST MR system phantom** (Russek et al., 2012)

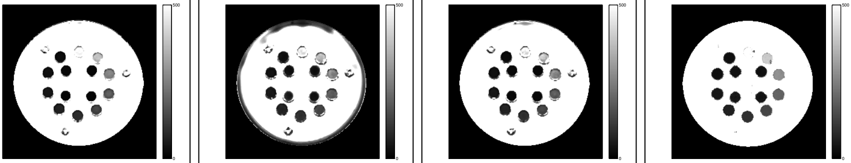


(a) $\widehat{\mathbf{T}}_1^{\mathrm{RLS}}$: (2 SPGR, 1 DESS) (b) $\widehat{\mathbf{T}}_1^{\mathrm{RLS}}$: (1 SPGR, 1 DESS) (c) $\widehat{\mathbf{T}}_1^{\mathrm{RLS}}$: (0 SPGR, 2 DESS) (d) $\widehat{\mathbf{T}}_1^{\mathrm{RLS}}$: (2 IR)

Figure 3: T_1 RLS phantom estimates. Colorbar range is $[0, 2000]$ms.

Phantom Results: T_2

Coronal scans of **NIST MR system phantom** (Russek et al., 2012)



(a) $\widehat{\mathbf{T}}_2^{\text{RLS}}$: (2 SPGR, 1 DESS)

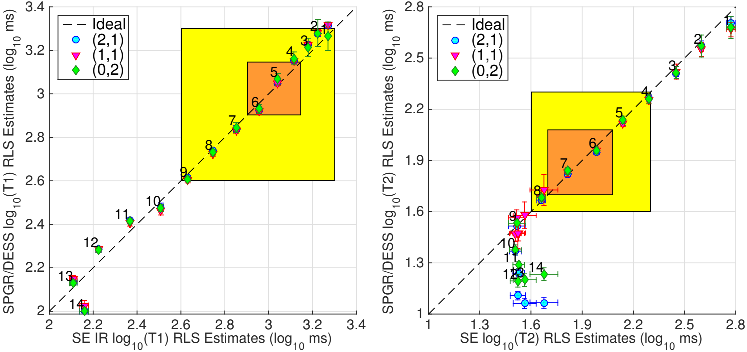
(b) $\widehat{\mathbf{T}}_2^{\text{RLS}}$: (1 SPGR, 1 DESS)

(c) $\widehat{\mathbf{T}}_2^{\text{RLS}}$: (0 SPGR, 2 DESS)

(d) $\widehat{\mathbf{T}}_2^{\text{RLS}}$: (2 SE)

Figure 4: T_2 RLS phantom estimates. Colorbar range is $[0, 500]$ms.

Phantom Results: Comparisons

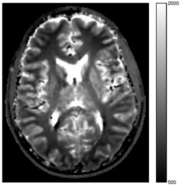


(a) $\widehat{T}_1^{\mathrm{RLS}}$ Estimates

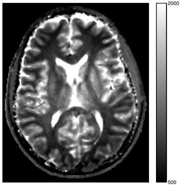
(b) $\widehat{T}_2^{\mathrm{RLS}}$ Estimates

Figure 5: Comparisons of T_1 and T_2 estimates from fast SPGR/DESS profiles versus slow IR and SE profiles, respectively. Within tight and broad ranges of interest, estimates in good agreement.

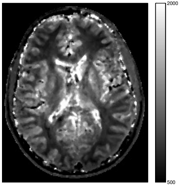
(Jeff's) Brain Results: T_1



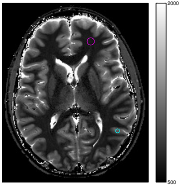
(a) $\widehat{\mathbf{T}}_1^{\text{RLS}}$: (2 SPGR, 1 DESS)



(b) $\widehat{\mathbf{T}}_1^{\text{RLS}}$: (1 SPGR, 1 DESS)



(c) $\widehat{\mathbf{T}}_1^{\text{RLS}}$: (0 SPGR, 2 DESS)

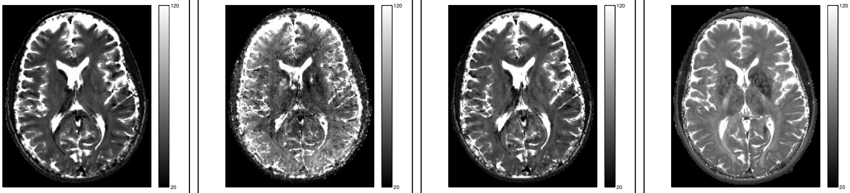


(d) $\widehat{\mathbf{T}}_1^{\text{RLS}}$: (2 IR)

Figure 6: T_1 RLS brain estimates. Colorbar range is $[500, 2000]$ms.

Scan	$(2,1)$	$(1,2)$	$(0,2)$	(2 IR)
WM $\widehat{T}_1^{\text{RLS}}$	773 ± 51	711 ± 53	721 ± 38	$660. \pm 13$
GM $\widehat{T}_1^{\text{RLS}}$	1110 ± 160	1110 ± 180	990 ± 110	1029 ± 39

(Jeff's) Brain Results: T_2



(a) $\widehat{\mathbf{T}}_t^{\mathrm{RLS}}$: (2 SPGR, 1 DESS)

(b) $\widehat{\mathbf{T}}_2^{\mathrm{RLS}}$: (1 SPGR, 1 DESS)

(c) $\widehat{\mathbf{T}}_2^{\mathrm{RLS}}$: (0 SPGR, 2 DESS)

(d) $\widehat{\mathbf{T}}_2^{\mathrm{RLS}}$: (2 SE)

Figure 7: T_2 RLS brain estimates. Colorbar range is $[20, 120]$ms.

Scan	$(2, 1)$	$(1, 2)$	$(0, 2)$	(2 SE)
WM $\widehat{T_2^{\mathrm{RLS}}}$	42.3 ± 3.3	48.5 ± 7.7	45.5 ± 3.6	61.9 ± 2.6
GM $\widehat{T_2^{\mathrm{RLS}}}$	54 ± 11	71 ± 11	54.7 ± 8.4	68.7 ± 5.0

Summary and Future Directions

Summary

- Introduced a CRB-inspired min-max approach to aid robust, application-specific MR scan design
- Practical application: optimized (SPGR, DESS) combinations for T_1, T_2 relaxometry in WM/GM regions of the brain
- Numerical simulations + phantom and brain experiments

Ongoing and Future Work

- Scan design for est. flip angle scaling $\kappa(\mathbf{r})$ also (Nataraj et al., 2014)
- Scan design when analytical signal model unknown

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   - Stephen Russek, Ph.D.
2. Daniel Weller, Ph.D. (U. Michigan, now UVA)

Figure 8: `http://collaborate.nist.gov/mriphantoms`

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