Quantitative Analysis of Dynamic Contrast-Enhanced MRI using R

The **dcemriS4** package

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1. Motivation
2. Dynamic Contrast Enhanced MRI
3. Parameter Estimation
4. Conclusions

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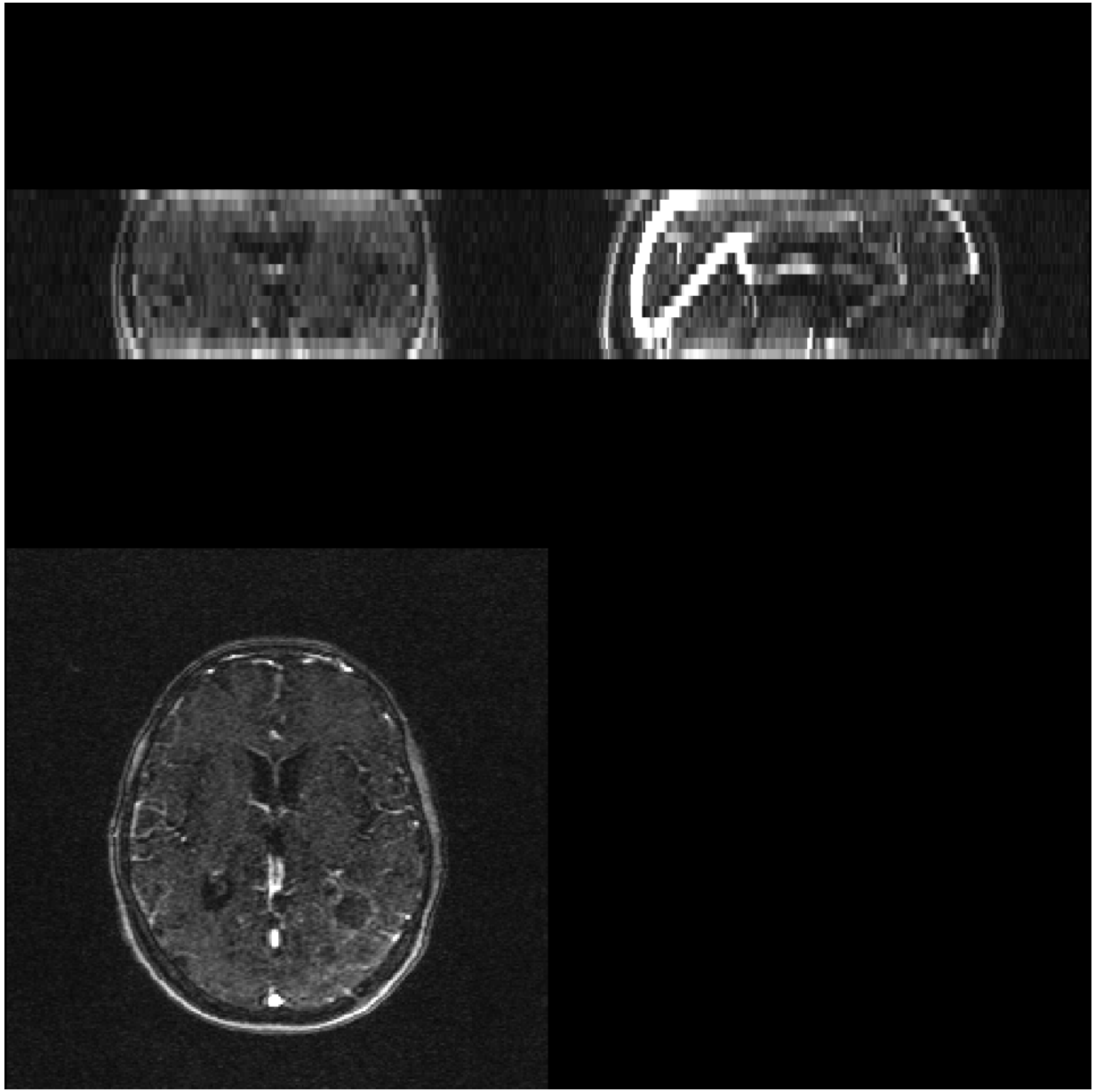
Introduction

- The quantitative analysis of DCE-MRI involves fitting pharmacokinetic (PK) models to the concentration of a contrast agent over time.
- Gadolinium-based contrast agents, involving a small molecular-weight substance, are injected after several baseline scans.
- Using T1-weighted sequences, the reduction in T1 relaxation time caused by the contrast agent is the signal dominant enhancement.
- T1-weighted kinetic curves have three major phases
  - the upslope
  - maximum enhancement
  - washout
- Dynamic acquisition
  - 5-10 minutes for oncology applications
  - 60-90 minutes for neurology (BBB) applications
- **dcemriS4** facilitates all stages of data analysis for DCE-MRI, and diffusion-weighted imaging (DWI), using S4 `nifti` objects.

RIDER Neuro MRI



Data Acquisition

1. Localizer
2. Structural scans
3. Multiple flip angles
4. B1 characterization (3T or higher fields)
5. Dynamic (bolus injection + 30s)
6. Structural scans
7. DWI

Data Acquisition

1. Motion correction and co-registration
2. T1 relaxation
3. Gadolinium concentration
4. B1 mapping
   - For higher field strengths (3T or more)
5. Arterial input function
6. Kinetic parameter estimation
7. Statistical inference

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Tips and Tricks

- Automation is the key to accurate and consistent results
- Quantitative analysis of DCE-MRI depends on several key acquisition parameters
- **oro.dicom** provides the facility of converting DICOM header information into a CSV file

```
path <- file.path(".")
subject <- 1086100996
dcm <- dicomSeparate(file.path(path, subject))
## Save DICOM header information to CSV file
dcm.csv <- dicomTable(dcm$hdr)
write.csv(dcm.csv, file=paste(subject, "csv", sep="."))
```

T1 Relaxation

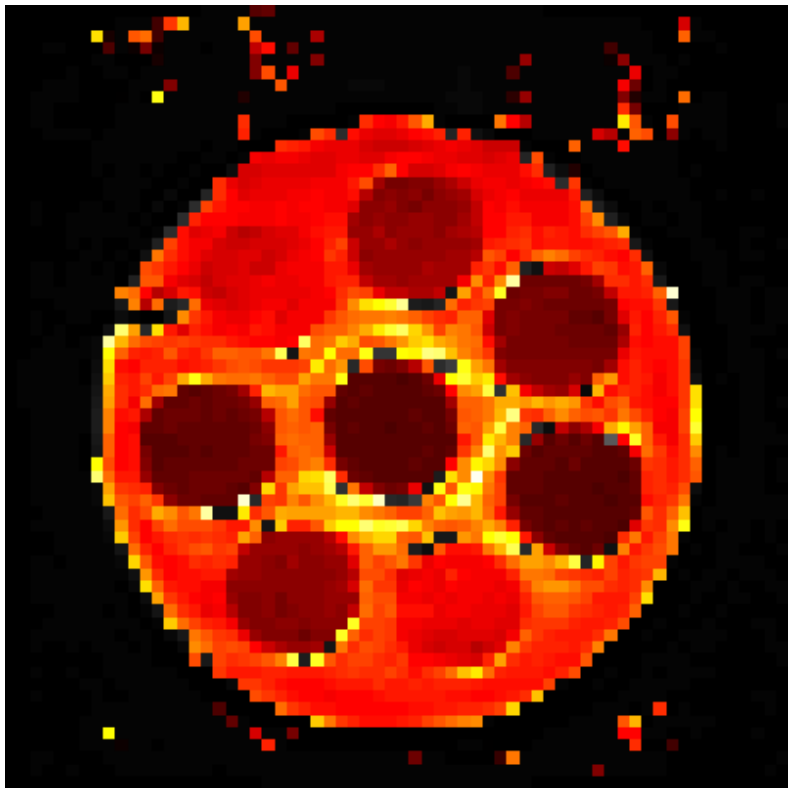

Figure: T1 Phantom

- Parametric form dictated by physics
- Multiple flip-angle acquisitions
- Nonlinear regression
  - Levenburg-Marquardt
  - **minpack.lm**
- B1 field correction is possible

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R code for T1 Estimation

```
R> alpha <- c(5, 10, 20, 25, 15)
R> TR <- 4.22 / 1000 # seconds
R> R1 <- R1.fast(flip, mask, alpha, TR, verbose = TRUE)
  Deconstructing data...
  Calculating R10 and M0...
  Reconstructing results...
R> overlay(vibe, 1/R1$R10[, , 1:nsli(vibe)], z = 13,
+     zlim.x = c(0, 1024), zlim.y = c(0, 2.5),
+     plot.type = "single")
```

- Flip angles in degrees
- Repetition time in seconds
- Signal intensities = 4D array
- Mask = 3D array
- Visualization provided by `overlay()` in **oro.nifti**

Arterial Input Functions

$$C_p(t) = D\left[a_1 \exp(-m_1 t) + a_2 \exp(-m_2 t)\right]$$

Variables

- $D = 0.1\text{mmol/kg}$, $a_1 = 3.99\text{kg/l}$, $a_2 = 4.78\text{kg/l}$, $m_1 = 0.144\text{min}^{-1}$ and $m_2 = 0.0111\text{min}^{-1}$
  - Weinmann *et al.* (1984); Tofts and Kermode (1984).
- $D = 0.1\text{mmol/kg}$, $a_1 = 2.4\text{kg/l}$, $a_2 = 0.62\text{kg/l}$, $m_1 = 3.0\text{min}^{-1}$ and $m_2 = 0.016\text{min}^{-1}$
  - Fritz-Hansen *et al.* (1996).

$$C_p(t) = A_B t \exp(-\mu_B t) + A_G\left[\exp(-\mu_G t) - \exp(-\mu_B t)\right],$$

Variables

- Orton *et al.* (2008)

Seed-based algorithm in `extract.aif()`

Kinetic Parameter Estimation

- The standard Kety (1951) model, a single-compartment model, or the extended Kety model, forms the basis for **dcemriS4**.

$$
\begin{aligned}
C_t(t) &= K^{trans}\left[C_p(t) \otimes \exp(-k_{ep}t)\right] \\
C_t(t) &= v_p C_p(t) + K^{trans}\left[C_p(t) \otimes \exp(-k_{ep}t)\right]
\end{aligned}
$$

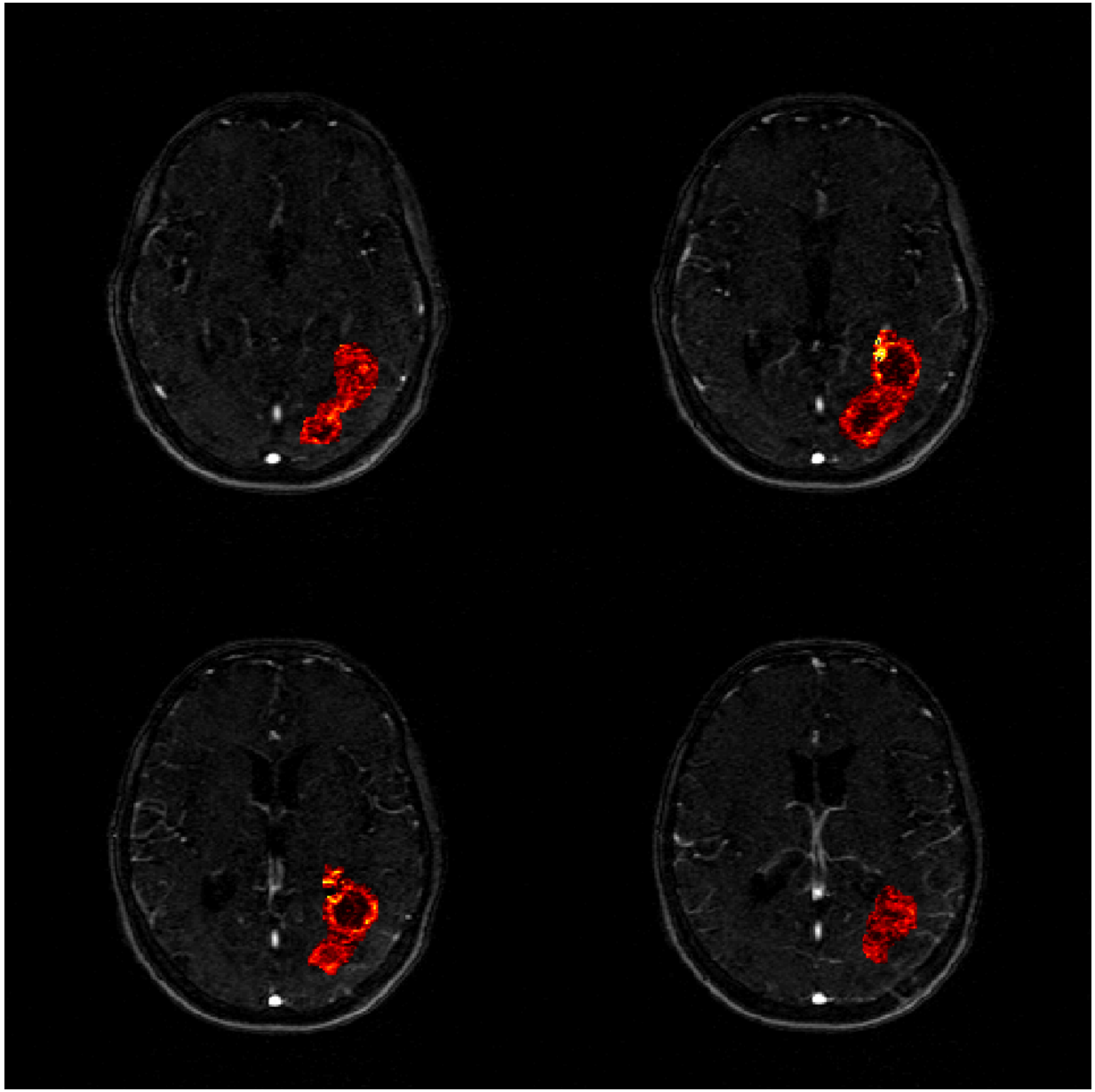
- Estimation techniques include:
  - Nonlinear regression (Levenburg-Marquardt, **minpack.lm**)
  - Bayesian estimation via MCMC (Schmid *et al.* 2006)
  - Bayesian estimation via MAP (adaptation of Schmid *et al.* 2006)
  - Bayesian estimation via penalized B-splines (Schmid *et al.* 2009a)
- Hierarchical Bayesian methods are not available at this time in **dcemriS4**, but will be in **PILFER**.
  - `http://pilfer.sourceforge.net`

Kinetic Parameter Estimation

```
acqtimes <- str2time(unique(sort(scan("rawtimes.txt", quiet=TRUE))))$time
conc <- readNIfTI(paste(s, d, "perfusion", "gdconc", sep="_"))
mask <- readANALYZE(paste(s, d, "perfusion", "mask2", sep="_"))
fit <- dcemri.lm(conc, (acqtimes - acqtimes[8]) / 60,
                 ifelse(mask > 0, TRUE, FALSE), model="extended",
                 aif="fritz.hansen", verbose=TRUE)
writeNIfTI(fit$ktrans, paste(s, d, "perfusion", "ktrans", sep="_"))
overlay(dyn[, ,6:9,],
        ifelse(fit$ktrans[, ,6:9] < 0.25, fit$ktrans[, ,6:9], NA),
        w=11, zlim.x=c(32,512), col.y=hotmetal(), zlim.y=c(0,.1))
```

- Acquisition times are found in the DICOM data
  - DICOM header fields are vendor dependent
  - Zero must be defined as time of gadolinium injection
- Mask was created in FSLView
- Visualization provided by `overlay()` in **oro.nifti**
- Time conversion provided by `str2time()` in **oro.dicom**

RIDER Neuro MRI: K^{trans}



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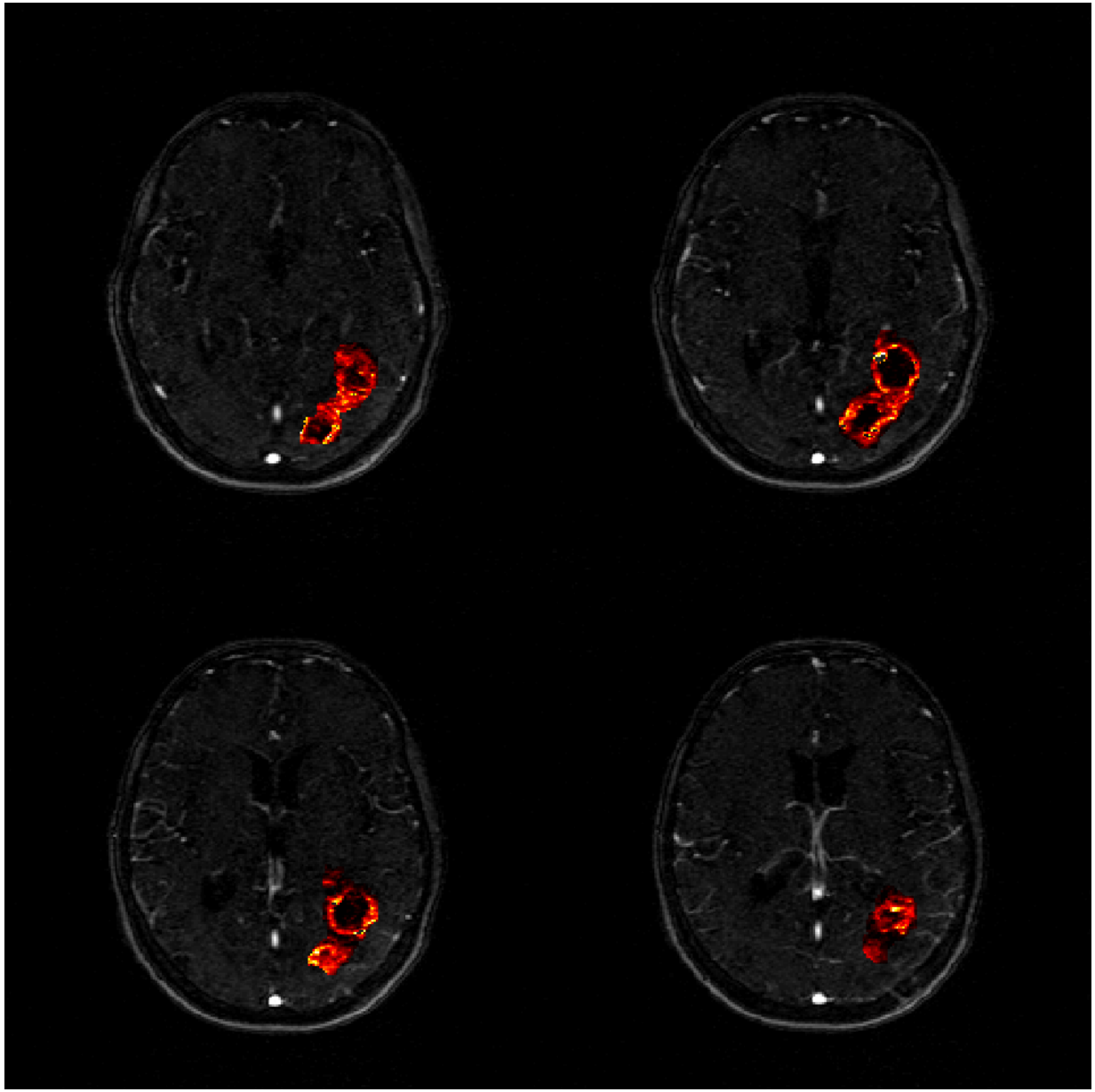
RIDER Neuro MRI: k_{ep}



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Statistical Inference

- Methodology for statistical inference is not included in the **dcemriS4** package.
- Please use the models/tests in **R** to perform hypothesis tests.
- Hierarchical Bayesian models are available, but not using **R**.
  - See Schmid *et al.* (2009b) for more information.

Conclusions

- The package **dcemriS4** attempts to provide quantitative methods for DCE-MRI
  - Vendor software (GE, Siemens, Philips, etc.)
  - Proprietary software (JIM, etc.)
  - Home-grown solutions
- Future directions
  - Multi-compartment models (Buckley *et al.*)
  - Parallelization (e.g., **multicore**)
  - Semi-parametric procedures (AUC, T_{max}, C_{max}, etc.)
- Feedback
  - Please provide feedback (pos/neg) on the SourceForge forum or mailing list.

References I

- Fritz-Hansen, T., E. Rostrup, *et al.* (1996). Measurement of the arterial concentration of Gd-DTPA using MRI: A step toward quantitative perfusion imaging. *Magnetic Resonance in Medicine*, **36**, 225–231.
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References II

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- Schmid, V. J., B. Whitcher, *et al.* (2009b). A Semi-parametric Technique for the Quantitative Analysis of Dynamic Contrast-enhanced MR Images Based on Bayesian P-splines, *IEEE Transactions in Medical Imaging*, **28** (6), 789–798.
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