Quantitative Analysis of Dynamic Contrast-Enhanced MRI using R
The \texttt{dcemriS4} package

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1 Motivation

2 Dynamic Contrast Enhanced MRI

3 Parameter Estimation

4 Conclusions
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
- **dcmriS4** 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
Tip 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.

```r
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

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

Figure: T1 Phantom
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
Parameter Estimation

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 \( m_2 = 0.0111\text{min}^{-1} \)
- \( D = 0.1\text{mmol/kg}, \ a_1 = 2.4\text{kg/l}, \ a_2 = 0.62\text{kg/l}, \ m_1 = 3.0\text{min}^{-1} \) and \( m_2 = 0.016\text{min}^{-1} \)

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

Variables

- Orton \textit{et al.} (2008)

Seed-based algorithm in \texttt{extract.aif()}
The standard Kety (1951) model, a single-compartment model, or the extended Kety model, forms the basis for \texttt{dcmriS4}.

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

Estimation techniques include:

- Nonlinear regression (Levenburg-Marquardt, \texttt{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 \texttt{dcmriS4}, but will be in \texttt{PILFER}.

- \url{http://pilfer.sourceforge.net}
Kinetic Parameter Estimation

acqtimes <- str2time(unique(sort(scan("rawtimes.txt", quiet=TRUE)))))$time
cconc <- readNIifTI(paste(s, d, "perfusion", "gdconc", sep="_"))
mask <- readANALYZE(paste(s, d, "perfusion", "mask2", sep="_"))
fit <- dcemri.lm(conc, (acqtimes - acqtimes[8]) / 60,
    ifelse(mask > 0, TRUE, FALSE), model="extended",
    aif="fritz.hansen", verbose=TRUE)
writeNIIfTI(fit$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: $K_{\text{trans}}$
RIDER Neuro MRI: $k_{ep}$
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 ($\text{AUC}$, $T_{\text{max}}$, $C_{\text{max}}$, etc.)

- Feedback
  - Please provide feedback (pos/neg) on the SourceForge forum or mailing list.


