QIBA DCE-MRI Synthetic Data

9/29/2011

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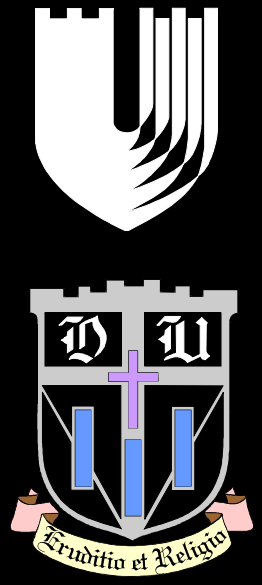


Disclosures

- Imaging core lab support from Eisai Pharmaceuticals, ACRIN, NIBIB / RSNA QIBA
- Member of GE Medical Systems Neuro MRI advisory board
- Pulse sequence support from Siemens Healthcare
- Dynamic contrast enhanced MR is an off-label use of gadolinium-based contrast agents

Justification

- DCE-MRI seen as a complex operation
- "A Rube Goldberg machine, device, or apparatus is a deliberately over-engineered or overdone machine that performs a very simple task in a very complex fashion, usually including a chain reaction. The expression is named after American cartoonist and inventor Rube Goldberg (1883-1970). Over the years, the expression has expanded to mean any confusing or complicated system."

Justification

- "It is recommended that a means should be explored for the major industry players to develop a process for evaluation of both acquisition and *analysis software* and make appropriate selections. "
  - ➔ Dynamic Contrast-Enhanced MRI--Meeting Report, CIP, Rockville MD, 11/2000
- Lack of standardized software still seen as a barrier to understanding the meaning of the parameters extracted, whether in clinical trials or in individual subjects: K^{trans}_{Duke} vs. $K^{trans}_{MD\ Anderson}$

Justification

- In order for DCE-MRI to be validated for clinical use, needs clear demonstration of utility as could be obtained in multi-center clinical trial
- Need to validate an approach from patient to quantitative metric
- Variation in software performance may be due to differences in solution algorithms, initial estimates, number of iterations, etc.

Important questions for DCE MRI analysis

- Which software package(s) to use?
- Does it make a difference?

DRO project – primary goals and objectives

- Overall goal: aid DCE-MRI analysis standardization by developing digital reference objects (DROs) simulating MRI with known parameters to evaluate and compare analysis implementations
- Provide **image datasets** and **verification protocols** to ensure that particular analysis packages can be used to extract K^{trans} and IAUGC with sufficient accuracy to meet claims of QIBA profile.

Profile description

- http://qibawiki.rsna.org/index.php?title=DCE-MRI_subctte
- **Quantitative microvascular properties, specifically transfer constant (K^{trans}) and blood normalized initial area under the gadolinium concentration curve ($IAUGC_{BN}$), can be measured from DCE-MRI data obtained at 1.5T using low molecular weight extracellular gadolinium-based contrast agents within a 20% within-subject coefficient of variation for solid tumors at least 2 cm in diameter.**
- Profile specified for use with: **patients with malignancy**, for the following indicated biology**: primary or metastatic**, and to serve the following purpose: **therapeutic response**.

Other QIBA activites

- Phantom development
  - ➔Accuracy of T_1 mapping
- Multi-center test-retest trial of DCE-MRI

Secondary benefits

- Aiding the process of software verification for software developers in the pre-release phase
- Supporting FDA approval of software packages
- Comparing the performance of software packages after release using identical input data.

Deliverables

1. Implementation of simple Tofts model DRO

   See https://dblab.duhs.duke.edu/modules/QIBAcontent/index.php?id=1
2. Verification of dcemriS4 package (http://www.dcemri.org)
3. Implementation of multi-flip T_1 mapping DRO
4. Extension of simulation to develop more realistic DROs
5. Development of verification protocols and integration into profiling activities
6. Creation of open source archives

Team introduction

- James MacFall, Ph.D. Duke
- David Radoff, M.S.

Open science paradigm

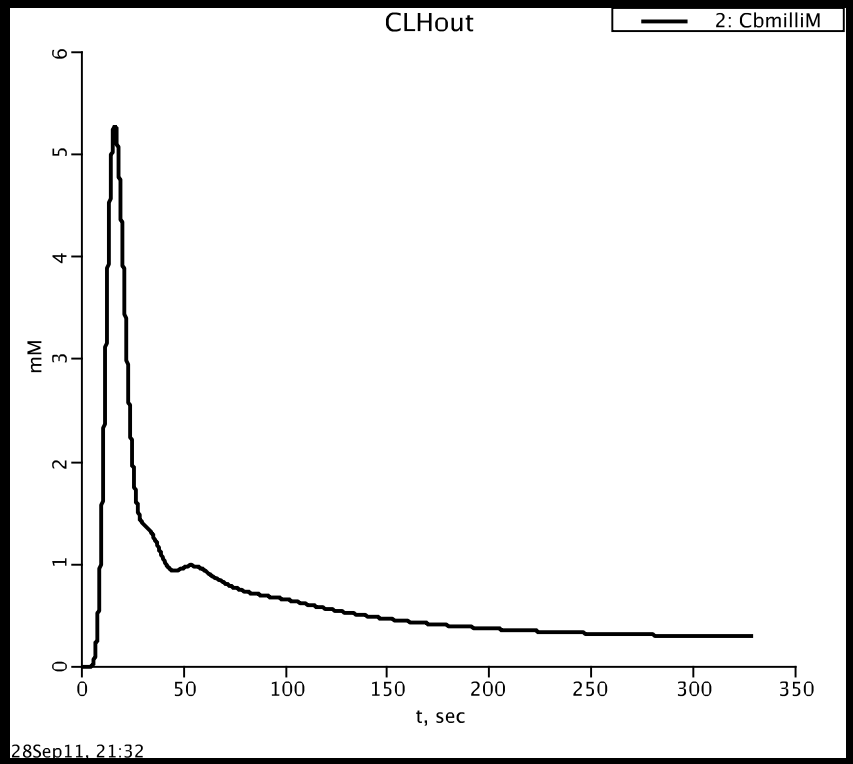
- Open source data
  - ➔XML and DICOM
- Open source software tools
  - ➔JSim (http://www.physiome.org/jsim/)
  - ➔dcemriS4 (http://www.dcemri.org)
  - ➔ImageJ (http://rsbweb.nih.gov/ij/)
  - ➔Dcm4che (http://www.dcm4che.org/)

Implementation of simple Tofts model DRO

- Need to simulate a particular protocol
- Described in QIBA documents here: http://qibawiki.rsna.org/index.php?title=MR_Acquisition_Protocols
- Has 5 flip angles: 3, 6, 9, 15, 24, 35 degrees
- TR 5 – 7 ms
- Dynamic images at 25 - 35 degrees
- 5.5 minutes of imaging
- Extract VIF from imaging data

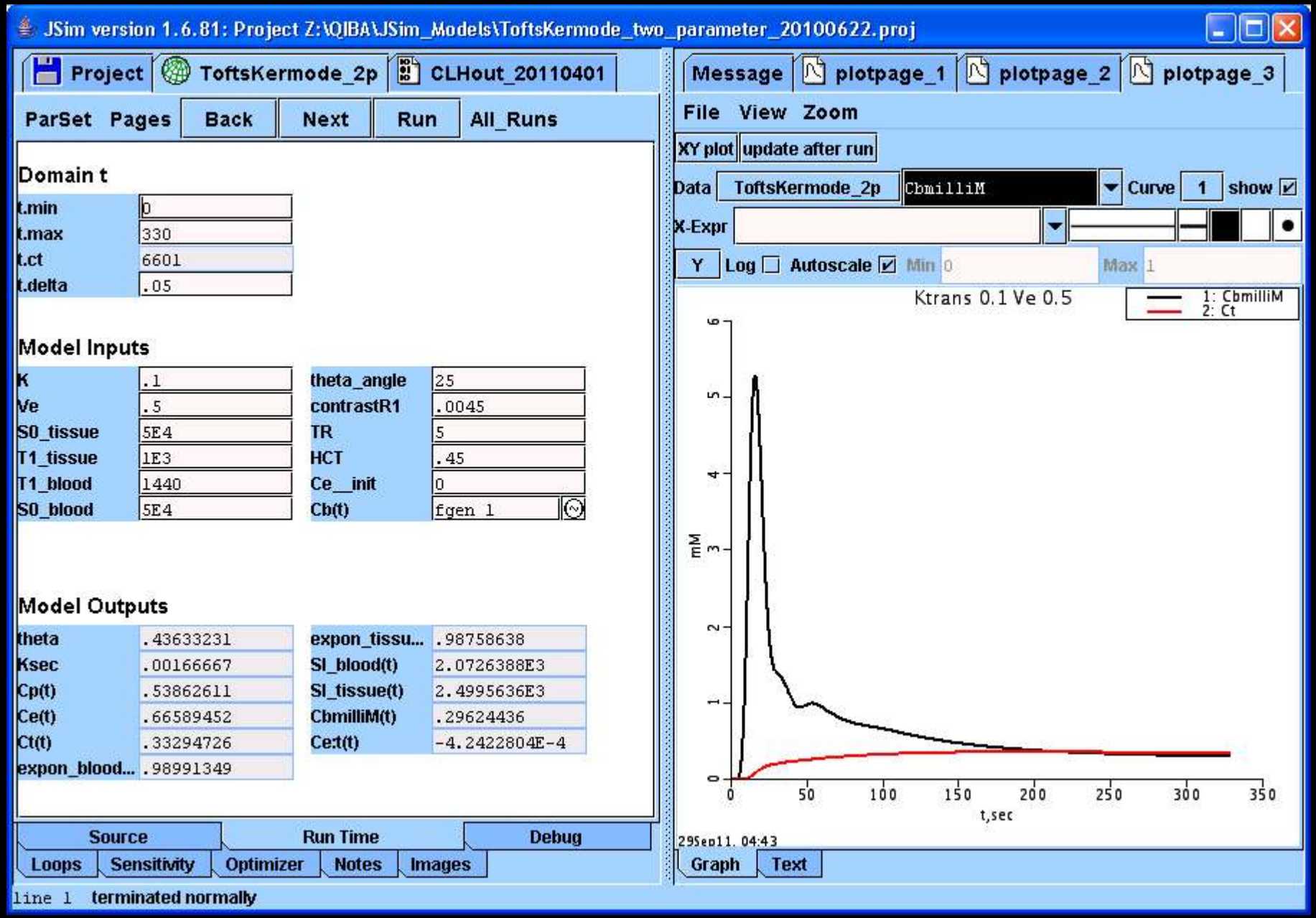
Implementation of simple Tofts model DRO

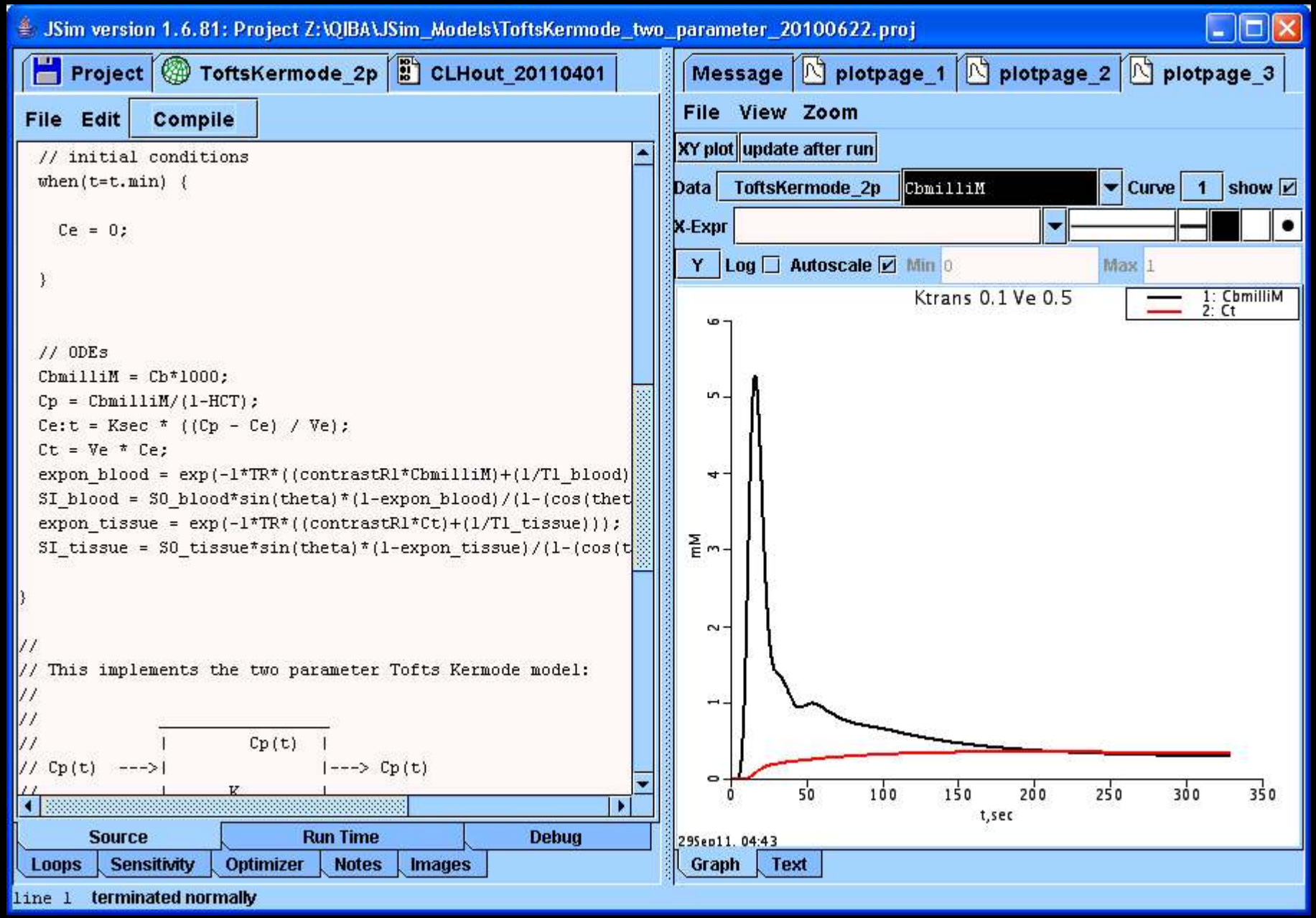
- Start with a synthetic input function (whole-body multi-organ model with delay/dispersion)
  Barboriak DP, MacFall JR, Viglianti BL, Dewhirst Dvm MW. Comparison of three physiologically-based pharmacokinetic models for the prediction of contrast agent distribution measured by dynamic MR imaging. J Magn Reson Imaging. 2008 Jun;27(6):1388-98
- Implemented as a JSim model and available on-line



Implementation of simple Tofts model DRO

- Create CTCs for tissues with K^{trans} = {0.01, 0.02, 0.05, 0.1, 0.2, 0.35} and v_e = {0.01, 0.02, 0.05, 0.1, 0.2, 0.5} using JSim

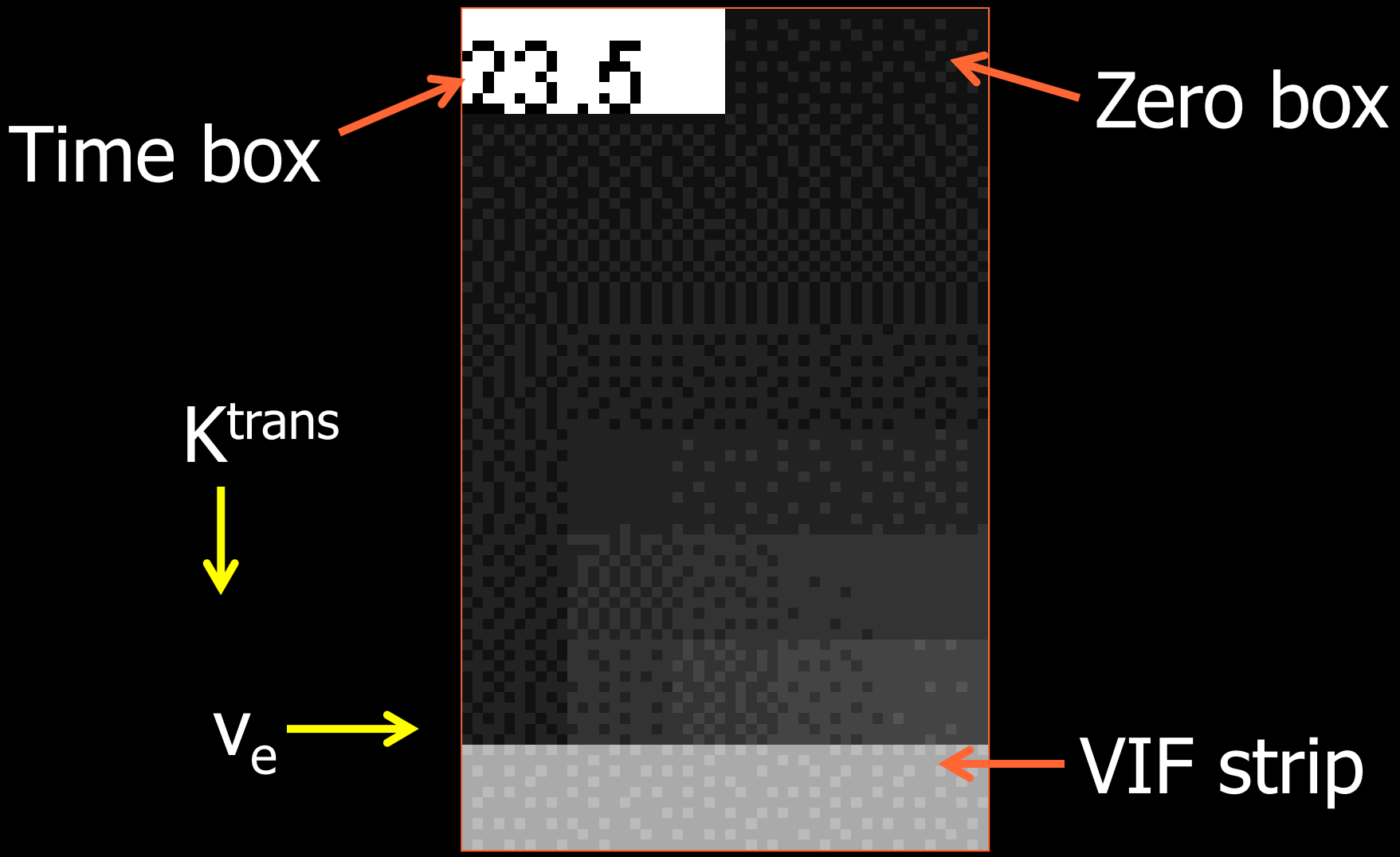

JSim version 1.6.81: Project Z:\QIBA\JSim_Models\ToftsKermode_two_parameter_20100622.proj
Project
ToftsKermode_2p
CLHout_20110401
ParSet Pages
Back
Next
Run
All_Runs
Domain t
t.min 0
t.max 330
t.ct 6601
t.delta .05
Model Inputs
K .1
Ve .5
S0_tissue 5E4
T1_tissue 1E3
T1_blood 1440
S0_blood 5E4
theta_angle 25
contrastR1 .0045
TR 5
HCT .45
Ce__init 0
Cb(t) fgen 1
Model Outputs
theta .43633231
Ksec .00166667
Cp(t) .53862611
Ce(t) .66589452
Ct(t) .33294726
expon_blood... .98991349
expon_tissu... .98758638
SI_blood(t) 2.0726388E3
SI_tissue(t) 2.4995636E3
CbmilliM(t) .29624436
Ce:t(t) -4.2422804E-4
Source
Run Time
Debug
Loops
Sensitivity
Optimizer
Notes
Images
line 1 terminated normally
Message
plotpage_1
plotpage_2
plotpage_3
File View Zoom
XY plot
update after run
Data ToftsKermode_2p
CbmilliM
Curve 1
show
X-Expr
Y Log Autoscale Min 0 Max 1
Ktrans 0.1 Ve 0.5
1: CbmilliM
2: Ct
mM
t,sec
0
50
100
150
200
250
300
350
1
2
3
4
5
6
29Sep11, 04:43
Graph
Text

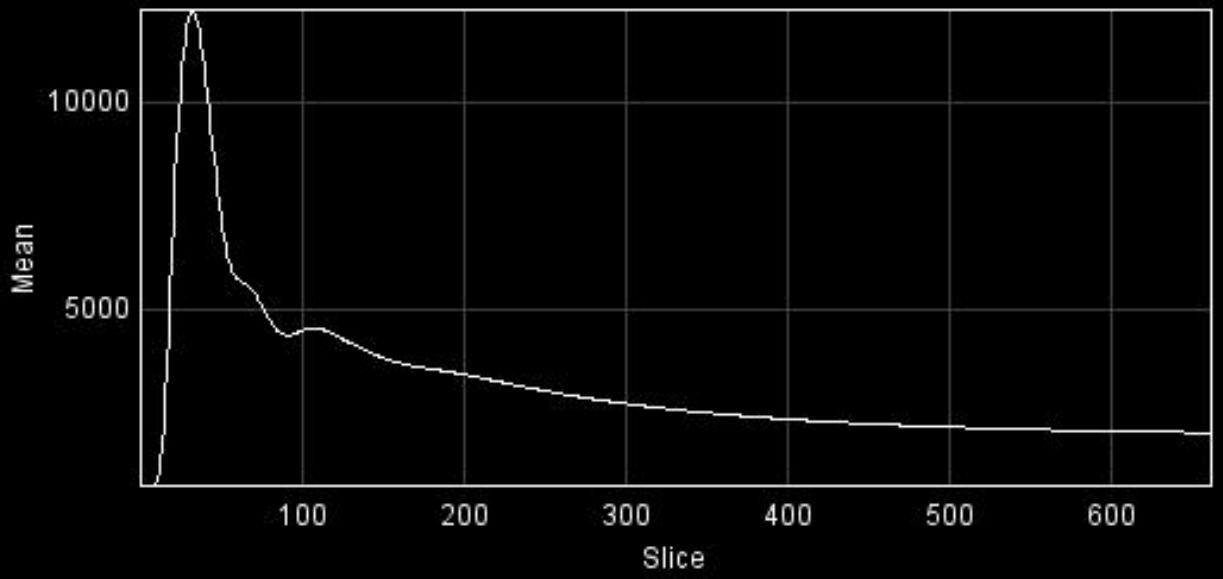

JSim version 1.6.81: Project Z:\QIBA\JSim_Models\ToftsKermode_two_parameter_20100622.proj
Project
ToftsKermode_2p
CLHout_20110401
File Edit Compile
// initial conditions
when(t=t.min) {
Ce = 0;
}
// ODEs
CbmilliM = Cb*1000;
Cp = CbmilliM/(1-HCT);
Ce:t = Ksec * ((Cp - Ce) / Ve);
Ct = Ve * Ce;
expon_blood = exp(-1*TR*((contrastR1*CbmilliM)+(1/T1_blood)
SI_blood = S0_blood*sin(theta)*(1-expon_blood)/(1-(cos(thet
expon_tissue = exp(-1*TR*((contrastR1*Ct)+(1/T1_tissue)));
SI_tissue = S0_tissue*sin(theta)*(1-expon_tissue)/(1-(cos(t
}
//
// This implements the two parameter Tofts Kermode model:
//
//
// Cp(t) ---> Cp(t) ---> Cp(t)
Source
Run Time
Debug
Loops
Sensitivity
Optimizer
Notes
Images
line 1 terminated normally
Message
plotpage_1
plotpage_2
plotpage_3
File View Zoom
XY plot
update after run
Data
ToftsKermode_2p
CbmilliM
Curve 1 show
X-Expr
Y Log Autoscale Min 0 Max 1
Ktrans 0.1 Ve 0.5
1: CbmilliM
2: Ct
mM
t,sec
0 50 100 150 200 250 300 350
0 1 2 3 4 5 6
29Sep11, 04:43
Graph
Text

Implementation of simple Tofts model DRO

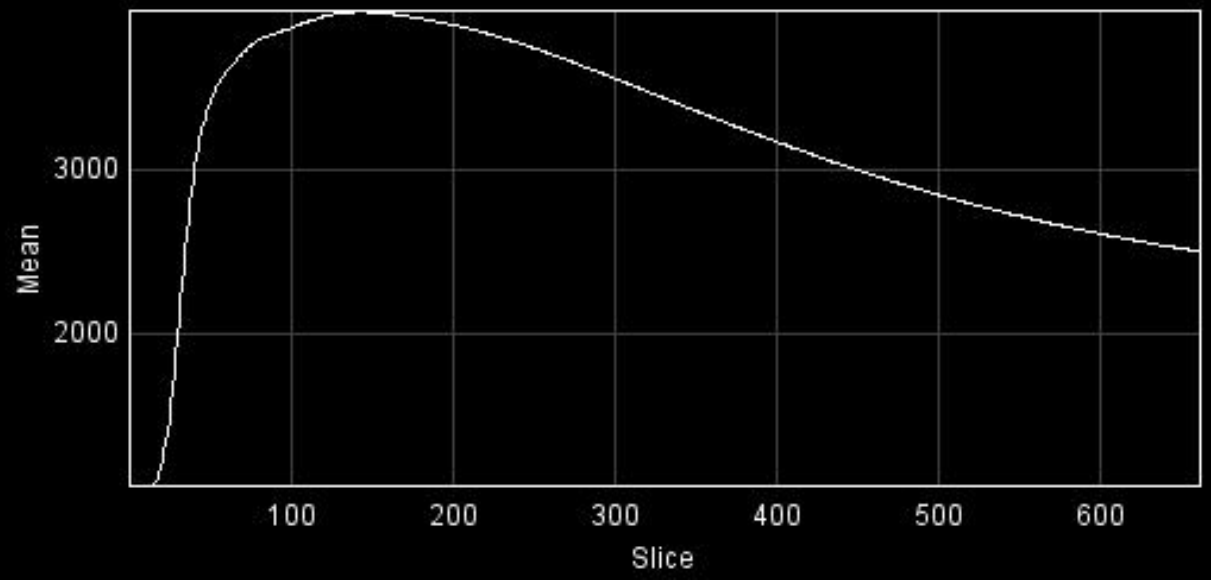
- Translate CTCs into SI vs. t curves
- For initial software testing, sample at unrealistically high rates (0.5 sec / image) and high equilibrium magnetization (50,000)
- 10 x 10 pixel tissue samples
- VIF strip
- XML, DICOM

Implementation of simple Tofts model DRO





VIF



K^{trans} 0.35,
v_e 0.5

Implementation of simple Tofts model DRO

- Data now released
- See beta version at http://dblab.duhs.duke.edu/modules/QIBAcontent/index.php?id=1

Verification of dcemriS4 package

- Background: Brandon Whitcher, Volker Schmid, www.dcemri.org
- Importance of open source packages
- A reference method (not "gold standard")
- An "open box" to compare to "black box" software
- Shape our expectations

Implementation of multi-flip T_1 mapping DRO

- Utility for QIBA
- Data is in the planning stages
- Proposal: T_1 {50 to 2000ms}, S_0 {1000 - 50,000}
- Patch size

Extension of simulation to develop more realistic DROs

- Consider software verification process as a series of hurdles
- Planning stages
- Reduce S_0
- Reduce sampling times
- Temporal jitter
- Add noise
  - ➔At some point, assumptions about VIF shape come into play
  - ➔Bias and reproducibility both become important

Development of verification protocols and integration into profiling activities

- The concept of "seal of approval" or "QIBA stamp"
- Challenge: summarizing multidimensional bias and reproducibility data into a "stamp" vs. "no stamp" decision
- Need for grading of "unknowns?"
- Are there tools we could use to automate iterative processes? CLIs? DICOM WG 23?

Creation of open source archives

- An area of active discussion
- Need to have an archive not only of DICOM, but XML, software and scripts

Other uses of synthetic data

- Investigations of alternative schemes
- A check for software in development phase
- Utility for FDA?
- All analyses fail at extremes: results may define the limitations of a given DCE-MRI acquisition technique

Community engagement

- Figures of merit for performance – the Rawlsian experiment
- Details of simulation extensions
- Automation tools – the "verification framework"

Communication

- Data, models etc: Barboriak lab: https://dblab.duhs.duke.edu/ Look for QIBA link on right
- QIBA DCE-MRI committee wiki: http://qibawiki.rsna.org/index.php?title=DCE-MRI_subctte
- QIBA synthetic data initiative: http://qibawiki.rsna.org/index.php?title=Synthetic_DCE-MRI_Data
- Discussion, comments: http://groups.google.com/group/qiba_dcemri_dro

In conclusion

- Your input will make the DROs more useful, thanks in advance for your interest and comments