Synthetic Data for DCEMRI Software Tool Validation: A Case Study

Sandeep N. Gupta[1] **Daniel P. Barboriak**[2]

[1] Visualization and Computer Vision Lab, GE Global Research, Niskayuna NY,
[2] Department of Radiology, Duke University Medical Center, Durham NC.

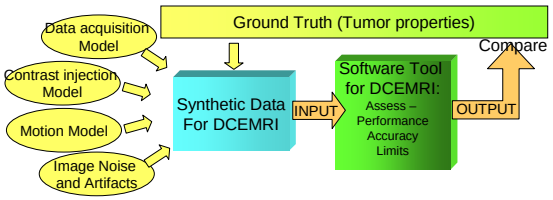
INTRODUCTION

Dynamic contrast-enhanced MRI (DCEMRI) is a non-invasive method for measuring vascular physiology by tracking the pharmacokinetics of low-molecular weight Gd-based contrast agents as they traverse tumor vasculature [1-2]. In a large number of single center studies, treatment of tumors has been associated with statistically significant changes in parameters derived from DCEMRI, and these have been shown to correlate with angiogenesis markers of MVD and VEGF expression [3-5].

Use of DCEMRI in large scale clinical trials has been hampered in large part due to two reasons: (a) Lack of robust and standard quantitative imaging protocols and sequences that permit accurate quantification of contrast agent concentration profiles; and (b) Lack of easy to use, validated commercial tools that provide a standardized and automated way of analyzing the wealth of imaging data even in presence of motion and other artifacts.

The ***Quantitative Imaging Biomarkers Alliance (QIBA)*** is an initiative sponsored by RSNA to advance quantitative imaging and imaging biomarkers. This alliance engages researchers and industry in a cooperative enterprise to facilitate translation of quantitative imaging techniques from research applications to clinically useful techniques.

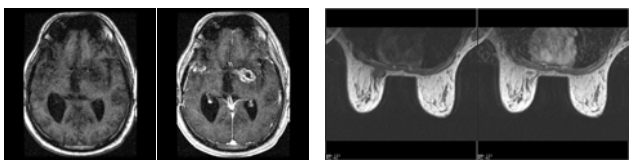
As part of this initiative, this work is aimed at demonstrating the value of synthetic data in software tool development and validation. The key benefit of using synthetic data is the explicit knowledge of gold standard ground truth which is not available in real-world clinical data. The workflow of the synthetic data model and use framework is shown in the schematic below.



DCEMRI IMAGING

DCEMRI Protocols: Standard DCEMRI protocol consist of a dynamic T1-weighted 3D gradient echo acquisition after the injection of a contrast agent. Typically 3-5 image sets are acquired prior to the contrast injection to allow a robust estimation of the signal baseline. Example protocol parameters:

3D Fast Spoiled Gradient Echo; TR/TE: 5.1/1.0 ms
Flip 25 deg; BW: +/- 31.25kHz; Matrix 256x160; FOV 28-40 cm
Gd DTPA 0.1 mmol/kg injected at 0.3 cc/sec for about 100 sec.



Example DCEMRI brain and breast images (pre and post contrast)

SYNTHETIC DATA

The QIBA version 4 synthetic DCEMRI images were used for the software verification For more information, please visit:

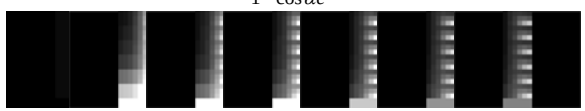
`http://dblab.duhs.duke.edu/modules/QIBAcontent/index.php?id=1`

Steps:

1. **Input Function:** An input function was derived from a physiologically-based whole body model of Gd distribution) [6] assuming a 0.1 mmol/kg dose for a 70 kg individual injected at 1.5 mmol/sec. This function was converted to a plasma concentration time curve assuming a blood hematocrit of 45%.
2. **Kinetic Parameters:** Using the General Kinetic Model (described below), tissue curves were generated for tissues using the following sets of parameters: K^{trans} {0,0.01,0.02,0.05,0.1,0.2}; f_{pv} {0.001,0.005,0.01,0.02,0.05,0.1}; v_e {0.1,0.2,0.5}. The values of these curves were extracted at 0.5 second intervals for a total of 660 images.

1. **DICOM Images:** The extracted values were used to create pixel-patches by converting into MR signal using the SPGR imaging equation below with: tissue T_1 1000 ms, blood T_1 1440 ms, TR 5 ms, α 25 deg, M_0 1000.

$$SI = \frac{M_0 \sin\alpha(1-e^{-TR/T_1})}{1-\cos\alpha e^{-TR/T_1}}$$



Example synthetic images from the data sets, showing a pre-contrast baseline image, and images from every 30 second time intervals.

DCEMRI ANALYSIS

We describe here the general 2-compartment model (also known as the Generalized Tofts-Kermode Model) describing contrast agent kinetics between the intravascular plasma space (where the agent is injected) and the extracellular extravascular space where the agent rapidly extravasates.

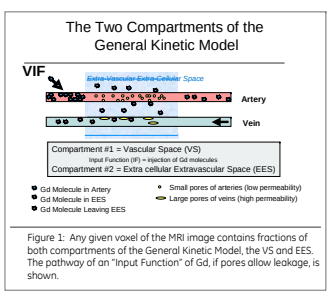


Figure 1: Any given voxel of the MRI image contains fractions of both compartments of the General Kinetic Model, the VS and EES. The pathway of an "Input Function" of Gd, if pores allow leakage, is shown.

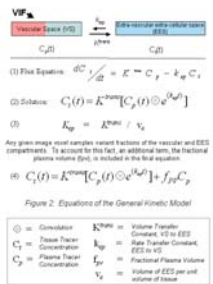
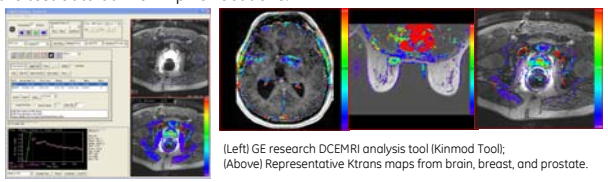


Figure 2: Equations of the General Kinetic Model

Analysis of DCEMRI data consists of first estimating the voxel concentration Ct and blood plasma concentration Cp from dynamic data, and then using Eq. 4 above to iteratively solve for best-fit parameters K^{trans}, k_{ep} (or v_e), and f_{PV}.

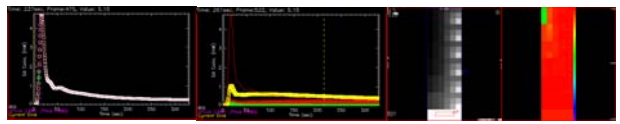
TOOL VALIDATION CASE STUDY

DCEMRI Analysis Tool: In this case study, we demonstrate the application of synthetic data described here for validation of a research prototype DCEMRI quantification tool (Kinmod Tool, GE Research). This tool implements the 2-compartment General Kinetic Model described before and allows for the measurement of an explicit vascular input function (VIF) which is embedded in the test data at known pixel locations.



(Left) GE research DCEMRI analysis tool (Kinmod Tool);
(Above) Representative Ktrans maps from brain, breast, and prostate.

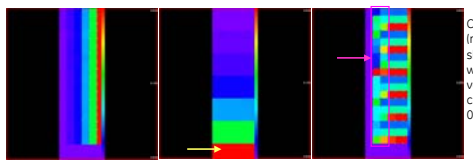
Validation Results: VIF was extracted from the data by a hand-drawn ROI placed in the known "vessel" region of synthetic data. Alternatively, automatic VIF detection algorithms can be used which work very well in these idealized conditions. Results of validation of estimated pixelwise pharmacokinetic parameters are shown below.



Extracted vascular input function from data (blood plasma concentration)

Representative uptake curves from regions of high (yellow), medium (red), and low (green) K^{trans}.

Original image (left) VIF ROI (red); Goodness of fit map (right) showing excellent fits (red color) except in upper left corner which has negligible signal due to ~0 K^{trans} and f_{PV}.



Computed K^{trans} (left), f_{PV} (middle) and ve (right) maps showing excellent match with ground truth, except in ve maps in the region corresponding to K^{trans} < 0.02 (purple box)

Quantitative comparison showed nearly perfect match between computed parameters and ground truth when K^{trans} was >= 0.02 /min. Note that fractional plasma volume was estimated as 1 in the region corresponding to VIF (yellow arrow) as expected. In regions where K^{trans} < 0.02, there is very small amount of leakage of the agent, and therefore ve maps yield large errors as it is not possible to reliably estimate the extracellular compartment volume when the contrast agent is not extravasating.

CONCLUSIONS

Synthetic test data can be used to help validate DCEMRI analysis software and to define ranges of parameters that are unlikely to yield accurate results. Future work will focus on evaluation of software packages with more realistic sets of synthetic images; for example, with more realistic time gaps between images and with added image noise and simulation of motion.

References

[1] *J Clin Oncol* 2006;24:3293-98.
[2] *Br J Cancer* 2007;96:189-195.
[3] *JMRI* 2001;14:237-242.
[4] *Abdom Imaging* 2004;29:166-72.
[5] *Acta Radiol.* 2005;46:353-58.
[6] *JMRI* 2008;27(6):1388-98.