Quantitative Analysis of Medical Imaging Data

Brandon Whitcher PhD CStat
Mango Solutions
London, United Kingdom
www.mango-solutions.com

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The Menu Today

- Motivation
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- Magnetic Resonance Imaging
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Motivation

- Search string = "imaging" on ClinicalTrials.gov
  - Found 30,801 studies with search of:
  - Found 2044 studies with search of: imaging
    - Hide studies that are not seeking new volunteers
    - Hide studies with unknown recruitment status

Imaging Biomarkers for Oncology

- The characterization of perfusion in tissue is a useful endpoint in clinical trials for drug development.
  - Antiangiogenic compounds
  - Vascular disruptive agents
- Imaging techniques may be used to assess perfusion non-invasively using exogenous and endogenous contrast.
  - Dynamic contrast-enhanced MRI
  - Dynamic susceptability-contrast MRI
  - Arterial spin labelling
- The characterization of *diffusion* in tissue has become a popular tool in the application of MRI.
  - Diffusion-weighted imaging (DWI)
  - Diffusion tensor imaging (DTI)

Imaging Biomarkers for Oncology

Compartmental Models in Medical Imaging

For example:

- Dynamic contrast-enhanced MRI for perfusion
- Kinetic modelling in dynamic PET
- Arterial spin labelling for perfusion

What is the experimental design?

- Duration
- Contrast agent

An approximation to the underlying biological system/process(es).

Magnetic Resonance Imaging

- A constant, homogeneous magnetic field (the B0 field) is used to polarize spins.
- The exposure of nuclei to a radio frequency (RF) pulse (the B1 field) at the Larmor frequency causes the nuclei in the lower energy state to jump to the higher energy state.
  - Macroscopic level: this causes net magnetization to spiral away from the B0 field.
  - After time, the magnetization vector becomes perpendicular to the main B0 field.
- MR imaging is based on the relaxation that takes place after the RF pulse has stopped.
- It is repeated for many different levels of phase encoding to build up a matrix in k-space.
- A 2D Fourier transform is performed, resulting in a single slice from an MRI acquisition.

Magnetic Resonance Imaging

Dynamic Contrast-Enhanced MRI

Dynamic Contrast-Enhanced MRI

Primary breast cancer example from the PSSC

K^{trans} v_e

Dynamic Contrast-Enhanced MRI

RIDER Neuro MRI data from Daniel Barboriak's lab at Duke

Dynamic Contrast-Enhanced MRI

The quantitative analysis of DCE-MRI data involves

1. Pre-processing of the T1 signal (e.g., motion correction, co-registration, correction of the B1 field)
2. Estimation of voxel-wise contrast agent concentration time curves
3. Determination of the arterial input function (AIF), either from the literature or by data-driven methods
4. Parameter estimation for a given compartmental model
5. Summary of voxel-wise estimates within the ROI
6. Statistical inference on kinetic parameters for differences between scans of a single patient or between distinct patients

Dynamic Contrast-Enhanced MRI

Usually in MR, one cites Kety (1951) for the model.

- "By building on the derivations of Bohr and Krogh it was possible to derive an expression for the exchange of an inert but diffusible tracer between flowing capillary blood and the surrounding tissue in terms of perfusion rate, the capillary diffusing surface, and the diffusion coefficient of the tracer through the capillary membrane (Kety, 1951)."

The History of Neuroscience in Autobiography, V1, (ed) LR Squire

Dynamic Contrast-Enhanced MRI

Whereas qPET studies routinely perform arterial cannulation to characterize the arterial input function (AIF) directly, it has been common to use literature-based AIFs in the quantitative analysis of DCE-MRI. Data driven AIFs are also utilized

$$C_p(t) = D\left(a_1 e^{-m_1 t} + a_2 e^{-m_2 t}\right).$$

The contrast agent concentration time curve at each voxel in the region of interest (ROI) is approximated using

$$\begin{aligned} C_t(t) &= K^{\text{trans}}\left[C_p(t) \otimes e^{-k_{\text{ep}} t}\right], \\ C_t(t) &= v_{\text{p}} C_p(t) + K^{\text{trans}}\left[C_p(t) \otimes e^{-k_{\text{ep}} t}\right]. \end{aligned}$$

Dynamic Contrast-Enhanced MRI

Parameter estimation may be performed using...

1. Non-linear regression using non-linear least squares
2. Bayesian *maximum a posteriori* (MAP) estimation
3. Fully Bayesian inference using Markov chain Monte Carlo
4. Deconvolution via curve fitting w/ Bayesian penalized splines
5. Numerical deconvolution for kinetic analysis
6. "Spectral analysis" (PET)
7. Bayesian hierarchical model

Discussion

- Compartmental models are utilized in many medical image experiments (MRI and PET)
- Research is, unfortunately, done in isolation
- Which is the best method?
  - Prior information
  - More complex models (demanding acquisition protocol)
  - Differentiating flow from permeability?
  - Smoothing
- What can we (image modellers) learn from pharmacometrics?
- How can we merge PK or PD information from imaging with non-imaging sources?
- PET biodistribution studies?
  - Small molecules versus large molecules