Dynamic Contrast Enhanced MRI (DCE-MRI):
From the Simplest to the Most Advanced DCE-Model

David L Buckley, PhD - Division of Medical Physics, University of Leeds, Leeds, U.K.

Outline

1. Tracer kinetics principles – the building blocks
2. Simple – 1 compartment model
3. More advanced - 2 compartment models
4. Most (?) advanced – distributed parameter and tissue-specific models

1. Tracer Kinetic Modeling

- Extracellular agents (such as Gd-DTPA\(^1\)) accumulate in the interstitium of many tissues (e.g. muscle) but do not cross the healthy blood-brain-barrier.
- Functional information may be obtained by treating Gd-DTPA as a tracer and following its kinetics (as opposed to the conventional ‘static’ approach, inject - wait – image once).
- After intravenous administration (normally in the form of a bolus) Gd-DTPA transits the venous and arterial system leaking from capillary beds wherever the endothelial cell junctions allow. It is excreted via the kidneys [1].
- The choice of imaging method is crucially dependent on what is to be measured and the rate of tracer delivery and uptake.
- When imaging tissues with leaky capillaries (e.g. tumors), measurements are typically made using rapid T1-weighted gradient echo sequences (often FLASH or turboFLASH).
  - Gd-DTPA in the plasma has a relatively small influence on the signal except where the vascular volume is large (e.g. in the kidney, heart or certain tumors).
  - Gd-DTPA in the interstitial space has a significant effect since this often represents a significant fraction of the tissue volume.
- The temporal sampling requirements vary enormously. For perfusion studies a sampling interval of ~ 1 s is required to measure the rapid transit of the Gd-DTPA bolus. For so-called permeability studies the uptake of Gd-DTPA may take several minutes and sampling rates can be reduced to tens of seconds or even minutes.
- Transport of Gd-DTPA can be described using a number of parameters:
  - Perfusion, \(F\) (or plasma perfusion, \(F_p\)); capillary permeability-surface area product, \(PS\) (a measure of vessel leakiness); plasma volume, \(v_p\), and interstitial volume, \(v_e\).
- When put together in a physiologic model (e.g. Fig. 1) and formulated in mathematical terms the tracer kinetic parameters provide a powerful tool for data analysis.

\(^1\) A number of extracellular agents behave very similarly. The term Gd-DTPA is simply used for the sake of convenience and is not an endorsement of Magnevist specifically.
Fig. 1 - The basic capillary-tissue exchange unit (after Kuikka [2]). Two spaces (plasma and interstitium) are separated by a semi-permeable membrane. The plasma volume is replenished by flow of contrast agent and a fraction of this, $E$, is extracted to the interstitium in a single pass.

- One way of describing the tracer kinetics is to calculate the convolution of the arterial input function (AIF, the concentration of Gd-DTPA in the plasma of the feeding artery) with the tissue impulse residue function (IRF), the theoretical response in the tissue to an infinitely tight unit bolus [3].

$$C_t(t) = F_p \cdot AIF \otimes R(t)$$

where $C_t(t)$ is the tissue concentration of Gd-DTPA, $F_p$ is plasma perfusion, $R(t)$ is the IRF and $\otimes$ is the convolution operator.

- The shape of the IRF can be determined in two ways:
  - No assumption about $R(t)$. Numerical deconvolution may be performed using $C_t$ and the AIF and this results in an estimate of $R(t)$ directly. This won’t be considered further.
  - Model assumed. A mathematical description of $R(t)$ may be derived and then data fitting (usually non-linear regression) to the $C_t$ and AIF data is used to estimate the model parameters.

2. The one compartment model

- A compartment is defined as a well-mixed space, where the tracer has a uniform concentration. It is characterized by a monoexponential IRF.

- The most common models used to describe $R(t)$ in dynamic contrast-enhanced (DCE)-MRI studies today [4] [5] [6] assume a mono-exponential form for $R(t)$:

$$C_t(t) = K^{\text{trans}} \cdot AIF \exp\left(-\frac{K^{\text{trans}} t}{V_e}\right)$$

where $K^{\text{trans}}$ is the volume transfer coefficient [7].

- While simple and straightforward to use interpretation of the resulting parameter $K^{\text{trans}}$ can be a challenge. It depends upon assumptions made about the tissue status; $K^{\text{trans}}$ may reflect $F_p$, it may reflect PS. More generally, it reflects a mixture of the two [8].
3. Two compartment models

- If the contribution of intravascular Gd-DTPA is thought to be significant, a second compartment is often added to the model. The simplest approach is often employed (e.g. [9]):

\[
C_i(t) = v_p \cdot AIF + K_{trans} \cdot AIF \otimes \exp\left(\frac{-K_{trans}t}{v_e}\right)
\]

- However, like the use of \(K_{trans}\), there are implicit assumptions in such an approach. In this case, the plasma transit time is assumed to be negligible [8]. There is evidence to suggest that this is often not the case [10,11].

- If this assumption is relaxed the 2 compartment model has a biexponential IRF and \(F_p\) and PS may be estimated separately [12]. Nevertheless, the data acquired may not have the necessary temporal characteristics or contrast-to-noise to provide precise estimates of the increasing number of parameters that result from the use of the 2 compartment model [13].

- It is possible to use statistical techniques to help in the selection of an appropriate model [11,14,15]. See Fig. 2.

Fig. 2 - The problem of model selection. DCE-CT data from a bladder tumour are poorly described by the 2-parameter 1-compartment model (left) and well described by a 4-parameter 2-compartment model (right). However, an F-test tells us that 3 parameters are sufficient to fit the data appropriately (centre).

4. Other models

- The ‘well-mixed’ assumption of a compartment, particularly with respect to the vascular space, can be avoided through use of distributed parameter models. These are now transferring from the fields of PET [16] and CT [17] into DCE-MRI [18]. While they have had limited exposure in the clinic to date, they show promise for the future [19,20].

- Measurement of liver perfusion is complicated by the organ’s dual blood supply (hepatic artery and portal vein). However, techniques have been developed to model this system [21,22].

- Another functional application of tracer kinetic modeling is the assessment of glomerular filtration rate (GFR) [23,24]. Gd-DTPA is filtered in the same way as many radioisotope markers of GFR and can be studied as part of a comprehensive renal exam [25].
Recommended Reading

Books:
A. Jackson, D.L. Buckley, G.J.M. Parker, Editors.
Dynamic Contrast-Enhanced Magnetic Resonance Imaging in Oncology

Review articles:
P.S. Tofts, Modeling tracer kinetics in dynamic Gd-DTPA MR imaging

A.M. Peters, Fundamentals of tracer kinetics for radiologists

S.P. Sourbron, D.L. Buckley, Tracer kinetic modelling in MRI: estimating perfusion and capillary permeability (Topical Review)

References


