Perfusion: DSC & DCE Basics & Analysis

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Highlight

Perfusion and perfusion-related parameters can be quantified using the contrast agent based methods DSC-MRI and DCE-MRI

Introduction

Perfusion is the term applied to capillary blood flow in tissue. Since the blood carries oxygen and nutrition to the tissue through the capillaries, perfusion is important in maintaining tissue viability. The study of brain perfusion has clinical applications due to the changes in perfusion associated with several neurological diseases. Diagnosis, lesion characterisation and follow-up of treatment in oncology, trauma, depression, dementia and acute ischaemic stroke are examples where assessment of the level of perfusion is of value. By using dynamic MRI in combination with an exogenous contrast agent, perfusion and perfusion-related parameters can be obtained.

Quantification of physiological parameters from contrast agent bolus tracking data is a two-step procedure. In the first step, the signal intensities from the experimental data are converted into contrast agent concentrations by employing MR signal theory. The second step aims to derive the relevant parameters from the time-resolved concentrations by means of tracer-kinetic theory. Dynamic Susceptibility Contrast MRI (DSC-MRI) and Dynamic Contrast Enhanced MRI (DCE-MRI) are two strategies that exist for retrieving contrast agent concentrations.

Dynamic Susceptibility Contrast MRI

By tracking the first passage of the contrast agent through the blood vessels in the brain using dynamic imaging and by applying kinetic models for intravascular tracers (Meier & Zierler 1954, Knutsson *et al.* 2010), perfusion and perfusion-related parameters such as cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) can be calculated using DSC-MRI. The injected contrast agent remains in the vascular compartment and this compartmentalization creates susceptibility gradients. The gradients cause local dephasing of the spins, leading to signal loss in T_2*-weighted MR images during the passage of the contrast-agent bolus. The contrast-agent concentration-time curves, C can be calculated from the signal–time course, S

$$C(t) = -\left(\frac{1}{k\,TE}\right) \cdot log\left(\frac{S(t)}{S_0}\right) \qquad [1]$$

where k is a constant, TE is echo time and S_0 is the baseline signal. Due to the duration of the intravenous injection and the vascular transport the contrast-agent bolus will not arrive at the brain as an infinitely narrow bolus, but will be distributed in time. By monitoring the concentration in an artery with time, the actual temporal distribution can be obtained. This arterial concentration curve is called the arterial input function (AIF). CBF is defined by the convolution:

$$C(t) = CBF\left[R(t) \otimes AIF(t)\right] \qquad [2]$$

where R(t) is the impulse tissue residue function describing the fraction of tracer still present in the vascular bed of the tissue voxel at time *t* after the bolus entered it. The CBV is given by

the time integral of C(t), normalised to the time integral of the AIF(t). Finally, MTT=CBV/CBF, according to the central volume theorem.

Dynamic Contrast Enhanced MRI

The blood-brain-barrier effectively confines contrast agent molecules to the vascular compartment. In case of its disruption, contrast agent may distribute into the extravascular, extracellular space (EES). By injecting a contrast agent and dynamically follow the bolus, often with spoiled gradient echo sequences, information about the hemodynamics in the microvasculature can be obtained using DCE-MRI.

The presence of the contrast agent will create an increase of the longitudinal relaxation rate $R_1=1/T_1$. The concentration C is proportional to the change in longitudinal relaxation rate, i.e., $C=(1/r_1)\cdot\Delta R_1$, where r_1 is the longitudinal relaxivity of the contrast agent.

The hemodynamic parameters are often obtained using curve-fitting approaches applied on the experimental data. Since a large number of unknown parameters might generate unreliable estimates it is common to include the effects of several physiological parameters into one parameter. The volume transfer constant of the contrast agent, K^{trans} [s^{-1}], between the blood plasma and the EES is such a combined parameter. The rate of tracer uptake in tissue (per unit volume of tissue) can be expressed as

$$\frac{dC_t}{dt} = K^{trans}\left(C_p - \frac{C_t}{v_e}\right), \qquad [3]$$

where C_t is tissue tracer concentration, C_p is tracer concentration in arterial blood plasma and v_e is the fractional EES volume. The physiological interpretation of K^{trans} depends on the relationship between capillary permeability and blood flow, F. For example, at high permeability, K^{trans} represents the plasma blood flow ($K^{trans}=\rho F(1-Hct)$ where ρ is the tissue density and Hct is the haematocrit), while in the other limiting case, when low permeability limits the tracer leakage, K^{trans} reflects the permeability-surface area product (PS) ($K^{trans}=\rho PS$). However, PS = 0 is not compatible with Tofts model (Sourbron & Buckley 2011).

The differential equation in Eq. 3 has the following solution (if $C_p = C_t = 0$ at $t = 0$):

$$C_t(t) = K^{trans}\int_0^t C_p(\tau)e^{-\frac{K^{trans}}{v_e}(t-\tau)}d\tau \qquad [4]$$

The equation, Tofts model (Tofts 1997) (also known as the Kety (Kety 1951) or Larsson (Larsson et al. 1994) model), states that the measured dynamic change in tissue concentration is modelled as a convolution of an exponential kernel and arterial blood or plasma concentration curve (i.e. AIF). If the blood volume cannot be neglected, a modified or extended Tofts model is applied by employing an additional term in Eq. 4, including the fractional plasma volume v_p and the arterial plasma concentration over time (Tofts 1997):

$$C_t(t) = v_p C_p(t) + K^{trans}\int_0^t C_p(\tau)e^{-\frac{K^{trans}}{v_e}(t-\tau)}d\tau \qquad [5]$$

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