Modelling in DCE-MRI

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Modelling of DCE (Dynamic Contrast-Enhanced) image data in MRI has enabled physiological characteristics of tumours and other lesions to be measured, as an aid to monitoring disease progress and treatment response. A contrast agent (CA; e.g. Gd-DTPA) is injected intravenously as a short bolus, and the subsequent enhancement in tissue signal in a T_1-weighted imaging sequence is measured. The widely-used one-compartment 'Tofts model' was first used in Multiple Sclerosis[1], was extended to include a vascular compartment[2], taken up by the cancer imaging community[3,4], and analysed in some detail to find its limits of validity[5,6].

The extracted (fitted) tissue parameters (transfer coefficient K^{trans}, extra-vascular extracellular space EES v_e, rate constant k_{ep} ($k_{ep}=K^{trans}/v_e$) and plasma volume v_p) are sensitive to some of the fixed parameters (tissue native T_1, called T_{10}, and relaxivity r_1 (change in $1/T_1$ per unit volume of CA)[3].

Quantification in medical imaging represents a paradigm shift[7]. Complex equipment can be used as a scientific instrument to make measurements (rather than to visualise in a qualitative way). To be an effective biomarker, a quantity should be i) biologically relevant ii) accurate (i.e. true) iii) reproducible (measured from repeated within-subject imaging). A *perfect imager* is one which contributes insignificant variance compared to the biological variance.

Recently these principles of modelling and quantification have been applied to the measurement of kidney function and vascularity[8]. The model takes account of the large vascular bed, and PC spreadsheet implementation is convenient. In healthy volunteers, values agree with those published using other methods. Reproducibility is acceptable (8-17%).

A crucial constraint to the model is to restrict time to the uptake portion, which in a large ROI lasts at least 90s. By avoiding efflux, the simplified model with a reduced number of free parameters has improved variance. ROI's larger than the nominal kidney outline enabled total filtration to be measured, unaffected by partial volume errors (the Object Strength approach[9].

Sensitivity analysis shows how fitted parameters are affected by the values of fixed parameters. T_{10}, r_1, MRI flip angle and haematocrit Hct are influential. Small vessels have reduced Hct compared to arteries (~24% vs. 42%) (the Fahraeus effect[10]). Thus measurements of *blood* volume and perfusion are uncertain, whilst *plasma* measurements are unaffected (since the CA resides in plasma; also in CT).

From these experiences in DCE-MRI a number of principles for modelling in a quantification procedure are clear:

1. relate the model to the known tissue physiology
2. use the simplest possible model that fits the data
3. ensure the fit is independent of starting values (use constraints)
4. identify the influential fixed parameters (related to the instrument, CA and tissue) and measure the sensitivity of the fitted parameters to these.
5. use repeated imaging (if possible) to estimate measurement variance
6. use phantoms (if possible) to measure accuracy[11]
7. output goodness-of-fit parameters (e.g. rms residual) and exclude fit failures
8. estimate (if possible) fitted parameter variance from Hessian (beware parameter covariance).

More material is on the websites qmri.org and www.paul-tofts-phd.org.uk (including pdf's of references)

(498 words)

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