A simple two-compartment model that describes Dynamic Contrast-Enhanced MRI signal in the kidney

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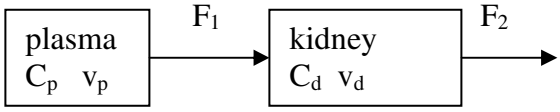
Hypothesis: Dynamic Contrast Enhanced (DCE) Gd imaging of the kidney can be analysed using a 2-compartment model and the concept of transfer constant K^{trans} that is established in tumours[1]

Introduction: DCE MRI of kidneys is becoming increasingly popular with the advent of fast sequences, and may replace conventional gamma camera and CT investigations, on the grounds of radiation dose and (in the case of the gamma camera) spatial resolution. Patlak analysis has been used traditionally[2], on the grounds of simplicity, although it has several conceptual problems when applied in a renal context. Efflux from the voxel must be ignored, and a subjective choice of the time interval over which a slope is calculated must be made. In addition, MRI signal nonlinearity is often ignored. Recent work[3,4] has shown the potential of a two-compartment approach. Here a simple, modern, spreadsheet based approach to compartmental modelling is explored.

Methods: **MRI:** 10 normal subjects were imaged before and after injection of 0.05 mmole/kg of Gd-DTPA, on a Siemens 1.5T Avanto imager, using a TIM 32 channel body phased array coil. A spoilt gradient echo 3D sequence had TR=1.6ms, TE=0.6ms, FA=17°. 18 contiguous 7.5mm slices were collected every 2.5s, with in-plane resolution 3.1 x 3.1mm, covering both kidneys. Images were spatially registered[5]. ROI's were placed on the descending aorta and a central slice in each kidney (cortex and medulla). Subjects were imaged a week later under conditions that were as identical as possible, giving a total of 40 normal kidney curves.
Compartmental Modelling: The simplest 2-compartment model for renal uptake has net tracer flow into the kidney as follows:

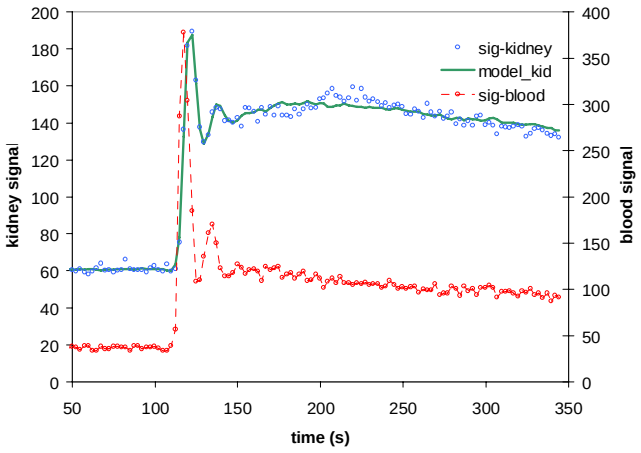
$$v_d \frac{dC_d}{dt} = F_1 - F_2 = K^{trans}C_p - K^{efflux}C_d$$

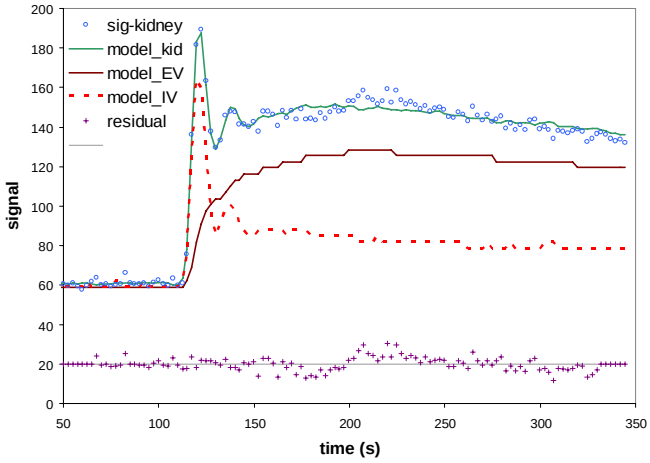
$$C_t = v_b(1-Hct)C_p + K^{trans}C_p \otimes e^{-k_d t} \quad ; \quad k_d = K^{efflux}/v_d$$



F_1 is the tracer extraction rate per unit volume (mmole min^{-1} ml^{-1}) from the plasma by the kidney; F_2 is the efflux (or *onward flux*) from the kidney voxel; K^{trans} is the transfer constant[1] from plasma to kidney (GFR per unit volume of tissue); K^{efflux} describes efflux proportional the renal concentration. v_p , v_b and v_d are the fractional volumes of plasma, blood and the distribution space for tracer extracted from the blood (principally the tubules). C_d, C_p, C_t are the time-dependent concentrations in v_d, plasma and kidney tissue respectively. The symbol $\otimes$ denotes convolution. $v_p=(1-Hct)v_b$, where Hct is the hematocrit. The newly-defined rate constant k_d depends on both efflux and the size of v_d. The solution is of the same mathematical form as in classic applications of Gd leakage such as tumours[1], although the significance of k_d is different. Delay (t_{del}), and dispersion of the bolus between the aorta and the kidney were also included[2].
MRI modelling. The blood signal was used to find C_p, taking into account signal nonlinearity with concentration[6]. The tissue signal was modelled using the standard expression for a spoilt gradient echo. Tissue parameters were: kidney T_1 =1.2s; blood T_1=1.4s; blood and tissue relaxivity r_1=4.5 s^{-1} mM^{-1}; Hct=41%. Fitting was carried out in a Microsoft Excel spreadsheet using the 'solver' add-in tool to minimise the residual sum of squares. There were 6 free parameters: the pre-Gd tissue signal, v_b, K^{trans}, k_d, t_{del} and a dispersion parameter.

Results: The 40 normal curves could all be reliably and quickly fitted by the model, with no evidence of systematic error. Rms signal residual was 2.5% of peak kidney value. Parameter values were (mean (sd)): K^{trans}: 0.48 min^{-1} (0.09); v_b: 0.38 (0.10); k_d : 0.78 min^{-1}(0.11).
Difference between repeated exams (rms value (CV)): K^{trans}: 0.14 min^{-1} (30%); v_b: 0.12 (32%); k_d : 0.14 min^{-1}(18%).





Discussion and Conclusions:

1. Excellent temporal and spatial resolution and coverage can be achieved in a modern 3D MRI acquisition.
2. This simple mathematical model captures the complexity of this DCE data, including bolus passage; a more complex model is unlikely to be justified.
3. Accounting for the delay and dispersion in bolus arrival improves the fit.
4. The inherent problems of the Patlak approach are overcome.
5. The normal K^{trans} values are consistent with established measurements of normal GFR (single kidney: GFR/unit volume ~ 60 ml min^{-1} / 150ml = 0.4 min^{-1}).
6. K^{efflux} can be estimated in normal kidney: if 80% of the extravascular space is accessible to Gd, then v_d=0.8*(1-v_b), K^{efflux} = v_d k_d = 0.8*(1-v_b)k_d = 0.39 min^{-1}. Without an efflux term (forcing k_d =0, i.e. using the Patlak model) the model showed clear deviation from the data even 30s after bolus arrival.
7. This model fits data from whole kidney ROI's. It needs evaluation for subregions and voxel mapping.
8. The model can easily be implemented in a spreadsheet, giving convenient access to ROI analysis in centres without computation resources.
9. Plotting intravascular (IV; v_b) and extravascular (EV; v_d) components, and residuals (vertically offset in the plot, for clarity), aids interpretation of the renal uptake curve (right hand figure)

References: 1. Tofts, JMRI 1999; 10:223 2. Prigent, Sem Nuc Med 1999; XXIX:146 3. Annet, JMRI 2004; 20:843
4. Buckley, JMRI 2006; 24:1117 5. Senneville, ISMRM 2006 6. Tofts, ISMRM 2007:2676 Funding from Kidney Research UK is acknowledged.