Estimating GFR from early (uptake) portion of DCE MRI renal data, using a 3-compartment model, improves reproducibility and may eliminate need for cortical segmentation.

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Hypotheses: 1) analysing the uptake-only (i.e. early) portion of Dynamic Contrast Enhanced (DCE) MRI kidney data will have benefits, since efflux is absent. 2) Larger Regions of Interest (ROI's), over-including the cortex and parenchyma, will estimate total slice GFR, with reduced dependence on ROI boundary.

Introduction: A 3-compartment model fits DCE data up to 3 minutes[1,2]; however there are two practical difficulties. (1) the stationary compartmental model includes efflux from tubules, however physiologically this cannot happen for at least 50-90s, and there is MRI evidence to support this[3]. (2) Defining a cortical ROI is an intricate operation, requiring significant prior knowledge, and with potentially large between-observer variation.

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. Subjects were imaged a week later, giving a total of 40 normal kidney curves.

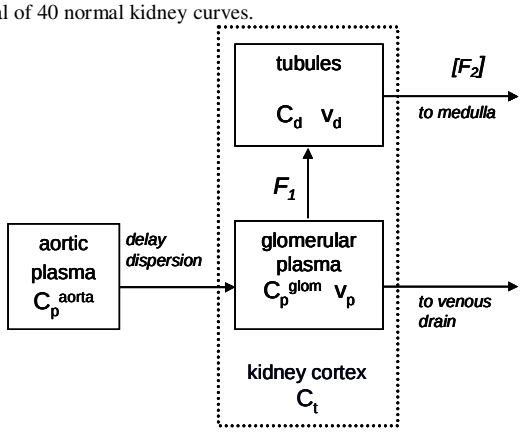
Compartmental Modelling: The simple 3-compartment model[2] for renal uptake has the following features.

$$C_p^{glom}(t) = C_p^{aorta}(t) \otimes g(t) = \int_0^t C_p^{aorta}(t-\tau) g(\tau) d\tau$$

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

$$v_d C_d(t) = K^{trans} C_p^{glom}(t) \otimes \exp(-K^{efflux} t / v_d)$$

$$C_t(t) = v_b (1 - Hct^{small}) C_p^{glom} + v_d C_d(t)$$



C_d, C_p^{aorta}, C_p^{glom}, C_t are the time-dependent concentrations in v_d, aortic plasma, glomerular plasma, and kidney tissue respectively. v_p , v_b and v_d are the fractional volumes of glomerular plasma, glomerular blood and the distribution space for tracer extracted from the blood (principally the tubules). The delay and dispersion[4] for plasma-borne tracer travelling from the aorta to the glomeruli are described the Glomerular Impulse Response Function (GIRF) g(t). F_1 is the tracer extraction rate per unit volume (mmole min^{-1} ml^{-1}) from the glomerular plasma by the kidney; K^{trans} is the transfer constant[5] from glomerular plasma to kidney (GFR per unit volume of tissue); F_2 is the efflux (or *onward flux*) from the kidney voxel, which in the model can be turned off ; K^{efflux} describes stationary efflux proportional the renal concentration. The symbol $\otimes$ denotes convolution. v_p=(1-Hct)v_b , where Hct is the hematocrit.

MRI modelling: Fitting was carried out in a Microsoft Excel spreadsheet[1]. There were 6 free parameters: the pre-Gd tissue signal, v_b, K^{trans}, K^{efflux} (which could be turned off), and delay and dispersion parameters. The GIRF was interpolated to a resolution of 0.2s before convolution.

MRI analysis: ROI's were placed on the descending aorta[6] . In a central slice in each kidney, seven ROI's were generated, ranging from a small piece of cortex to one that over-included the whole kidney (whilst excluding adjacent organs such as liver and spleen). Datasets with duration 50-100s after initial tracer arrival at the aorta were analysed. Total GFR for a ROI ($GFR_{ROI} = K^{trans} V_{ROI}$), where V_{ROI}=area of ROI x slice thickness, was calculated.

Results: Rms signal residual (n=40) was <2% of peak kidney value, gaussian GIRF's fitted best, and fitting took <5s. Parenchymal data could be fitted up to 90s with efflux turned off, and K^{trans} values were about 50% of those obtained by fitting a longer dataset with efflux turned on (suggesting model degeneracy with efflux on).

Normal parameter values were (mean (sd)): K^{trans}: 0.25 min^{-1} (0.04); v_b: 0.42 (0.10); GIRF delay 2.7s (1.05); perfusion 210 ml min^{-1} (100 ml)$^{-1}$ (67).

Difference between repeated exams (rms value (CV)): K^{trans}: 0.05 min^{-1} (20%); v_b: 0.10 (22%); GIRF delay 0.7s (26%); perfusion 41 ml min^{-1} (100 ml)$^{-1}$ (19%).

Plots of GFR_{ROI} showed a distinct plateau at large ROI sizes, whilst K^{trans} values for cortical ROI's (up to 400 pixels) were more variable (fig 2).

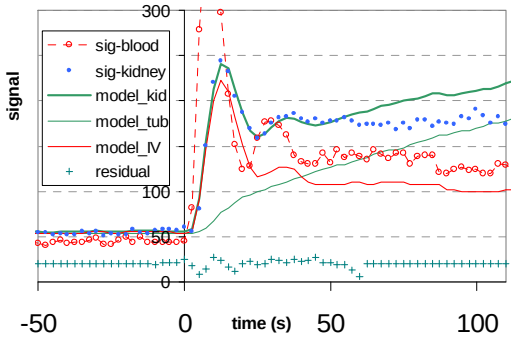


Fig 1: efflux-off fit to cortical ROI, showing efflux after 55s

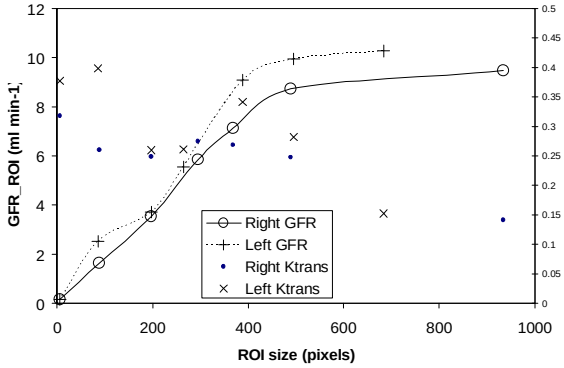


fig 2: estimates of GFR_slice and K^{trans} for a range of ROI's

Discussion and Conclusions:

1. Fitting the uptake-only portion gives reliable estimates of K^{trans}, using the simplified model with efflux turned off, and K^{trans} reproducibility[1] is improved.
2. The onset of tracer efflux can be seen by monitoring the residuals from the 'efflux-off' fit (fig 1). With efflux, signal is below that predicted by the model.
3. Slice GFR is approximately independent of ROI size, if the ROI over-includes all parenchyma, as expected from Object Strength studies of partial volume[7]
4. RBF and transit time estimates are available from the GIRF estimate, in spite of the limited temporal resolution of the data (2.5s).

References: 1. Tofts ISMRM 2008; 454 2. Tofts ESMRMB 2008; 36 3. Hackstein JMRI 2005; 22:406 4. Annet JMRI 2004; 20:843
5. Tofts JMRI 1999; 10:223 6. Mendichovszky Europ J Rad 2008 doi:10.1016/j.ejrad.2008.09.025 7. Tofts MAGMA 2005; 18:162