Accurate and precise measurement of renal filtration and vascular parameters using DCE-MRI and a 3-compartment model.

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Overview

A simple model of the renal uptake curve enables four key physiological parameters to be accessed.

K^{trans} filtration (GFR/unit volume) → GFR

v_b blood volume %

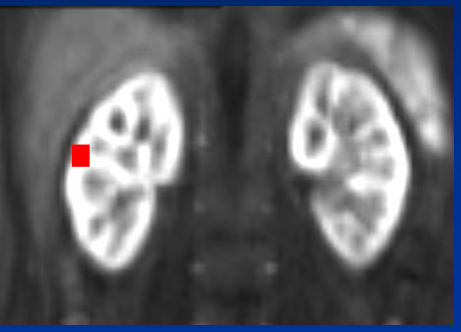
F perfusion ml blood (100 ml tissue) min-1

FF filtration fraction $FF = K^{trans} /((1-Hct)*F)$

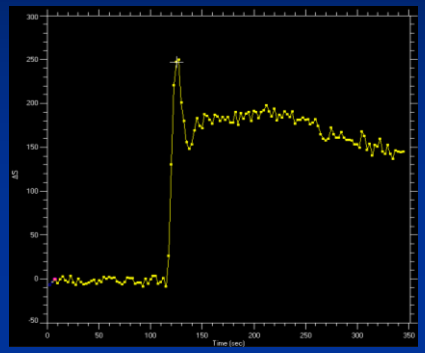
15 normal subjects were each imaged twice, to enable reproducibility to be measured (Bland-Altman analysis)

Accuracy by comparison with published values

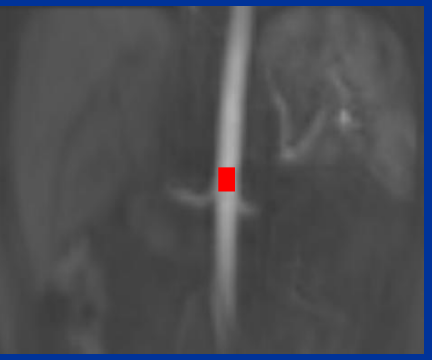
MRI Acquisition



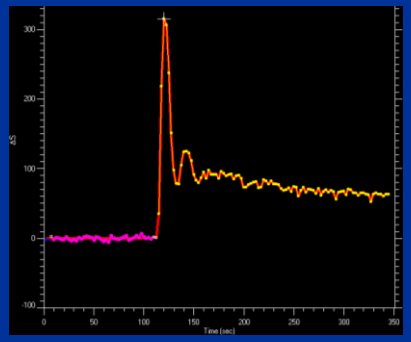
Cortical ROI



Time of peak



Arterial ROI



Arterial Input Function AIF

- Siemens Avanto 1.5 T scanner
- Abdominal TIM coil
- Gradient-echo 3D-FLASH pulse-sequence
- TR = 1.63 ms; TE = 0.53 ms
- Flip angle = 17°
- Strong fat saturation; PAT factor = 2 (GRAPPA)
- FOV = 400 x 325 mm^2
- 18 x 7.5 mm **coronal slices** covering entire kidney (no gap)
- Voxel size = 3.1 × 3.1 × 7.5 mm^3
- Frames acquired every 2.5 s
- Gd dose = 0.05 mmole/kg (**half dose**)

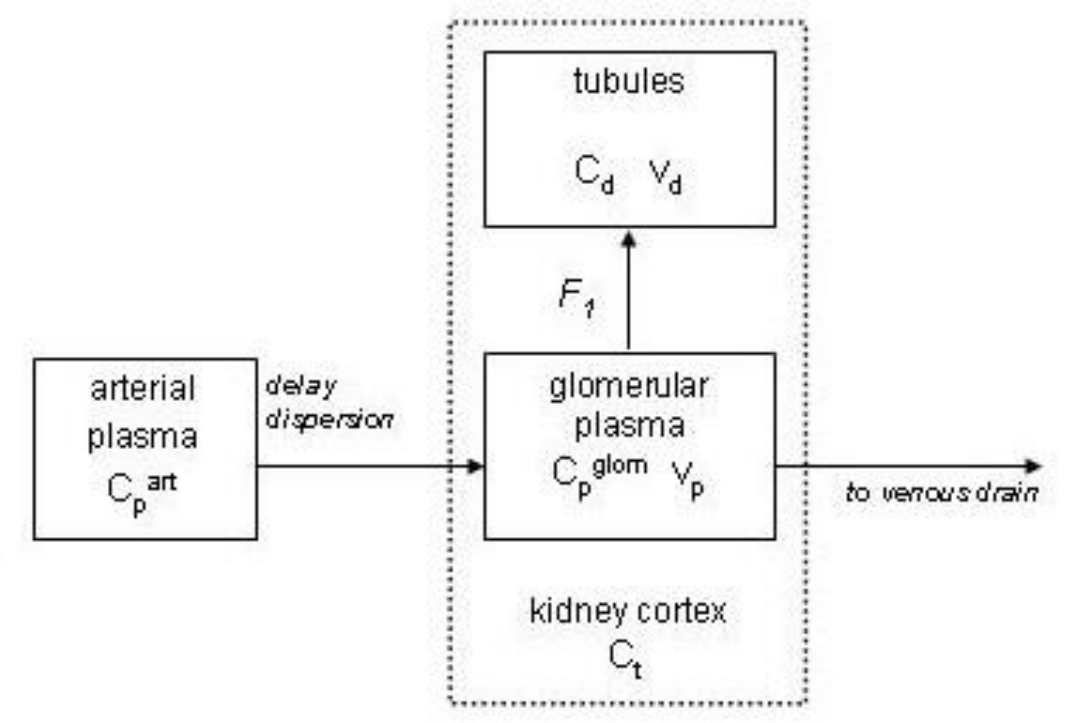
Kidney model

Uptake mode

no efflux from tubules (t<90s)

K^{trans} = transfer constant from plasma to kidney

(=GFR per unit volume of tissue)



glomerular plasma

g(t) = Glomerular Input Response Function

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

tubular tracer C_d

$$v_d \frac{dC_d}{dt} = F_1 = K^{trans} C_p^{glom}$$

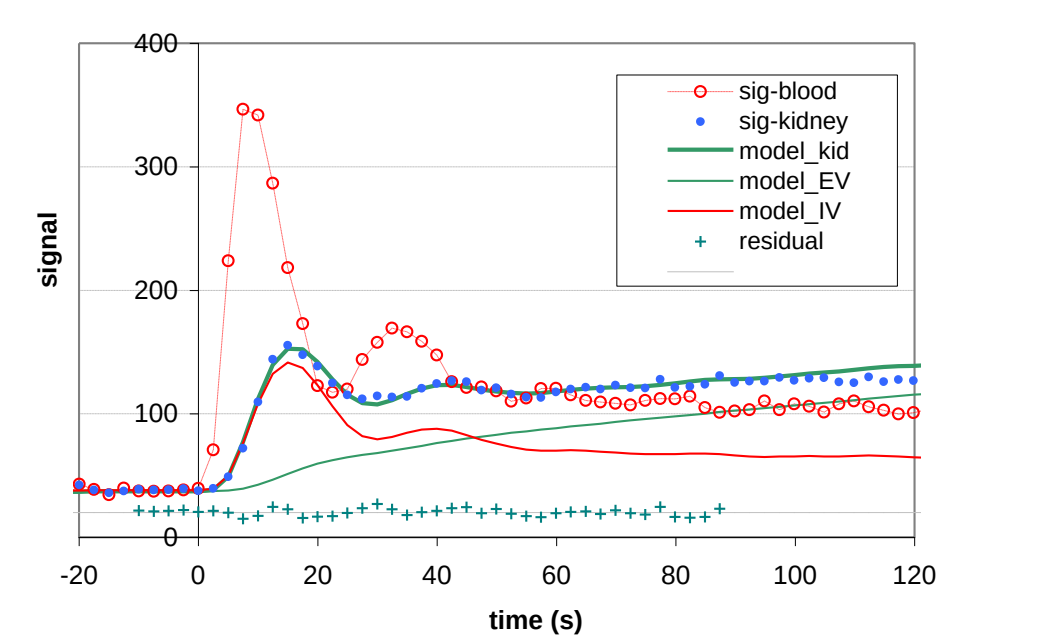
$$v_d C_d(t) = K^{trans} \int_0^{\tau} C_p^{glom}(\tau) d\tau$$

total tracer C_t

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

Fit parenchymal ROI
(uptake mode – no efflux)

- Spreadsheet implementation
  - uses solver; ROI fits in 5s
- blood and kidney signals
  - red circles; blue circles
- Fit up to 90s
  - green line
  - residuals RMS < 3%;
    - model errors are small
    - contributions from movement
    - contribution from blood signal noise?
  - efflux visible after 100s
    - kidney signal < model
- plot shows Gd in two compartments:
  - IV glomerular (red line; delayed AIF)
  - EV tubular (green line; shows uptake)



Error Propagation and choice of fixed parameters

- How dependant are the *fitted* parameters (filtration, vascularity) on the *fixed* parameters (haematocrit, relaxivity, T_{10}) ?

- Error Propagation Ratio
  - % change in fitted parameter for 1% change in fixed parameter

- Reducing Hct^{small} from 41% to 24% reduces v_b, F
  - improves accuracy

- Reducing tubular relaxivity r_1^d from 4 s^{-1} mM^{-1} to 1 s^{-1} mM^{-1} (suggested by rat work) increases K^{trans} ×4
  - implausibly high K^{trans}
  - unresolved mystery – true value of r_1^d ?

- Increasing kidneyT_{10} reduces filtration and F estimates
  - measure T_{10} if disease is present

- Mean Arrival Time MAT is robust
  - unaffected by choice of fixed parameters

	K^{trans}	v_b	F	MAT	FF
Fixed tissue parameters					
Hct^{large}	-0.72	-0.69	-0.70	0	0
Hct^{small}	0	+0.69	+0.69	0	0
r_1^{blood}	+0.98	+1.03	+1.03	0	0
r_1^{d}	-0.97	0	0	0	-0.99
r_1^{glom}	0	-0.98	-0.98	0	+0.99
$r_1^{glom} = r_1^{blood}$	+0.99 [c]	0	0	0	+0.99
T_{10}^{blood}	+1.04	+1.24	+1.29	0.02	-0.22
T_{10}^{kidney}	-1.06	-1.08	-1.14	0	+0.22
Fixed instrumental parameters					
θ	-0.07	+0.25	+0.29	0.03	-0.38
TR	0	-0.13	-0.15	0	+0.16

Table: error propagation ratios

Estimation of Glomerular Impulse Response Function

- GIRF = Response in glomeruli to concentration spike in aorta

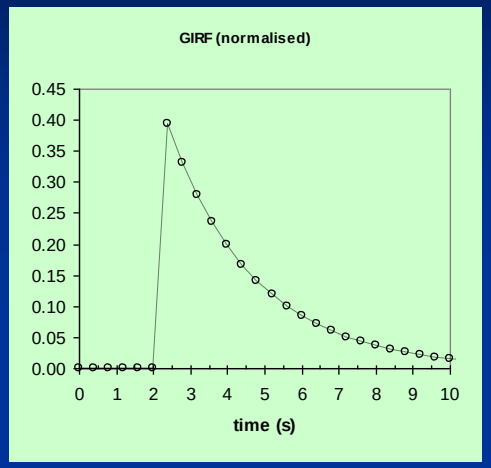
- Delayed exponential and delayed gaussian GIRFs fit well
  - Instant exponential GIRF fits worse

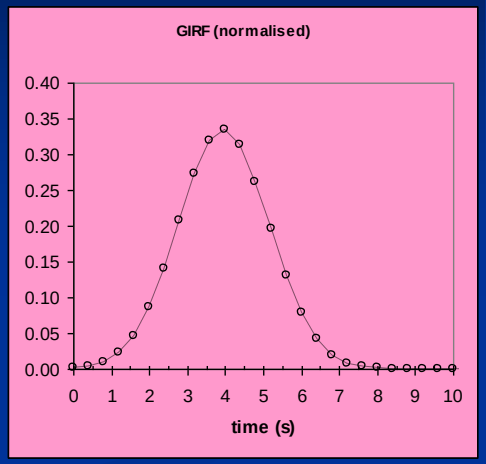
- Dispersion in vascular bed makes gaussian more plausible
  - Especially in large ROI
  - Tissue IRF measured by Sourbron; initial peak of this is vascular (i.e. GIRF) and looks gaussian

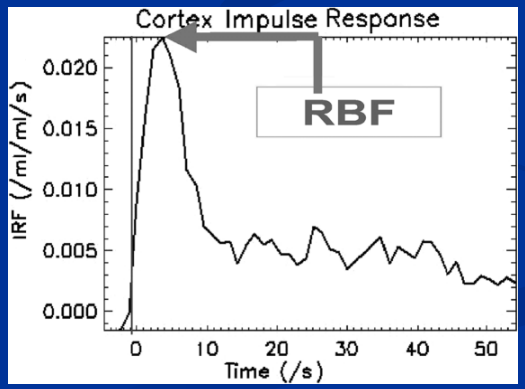
- Perfusion F estimation.. is tricky
  - From peak of exponential
    - Valid for gaussian??
  - From Mean Arrival Time
    - $F = v_b/MAT$?
  - All 4 methods have similar precision

- Accuracy is desirable
  - Gain clinical acceptance

- We have used peak of gaussian GIRF







Dujardin JMRI 2009

	peak	MAT
exponential	451	430
gaussian	282	450
literature	258	

F ml blood (100 ml tissue) $^{-1}$ min $^{-1}$
Parenchymal ROI; Hct=41%

Normal values

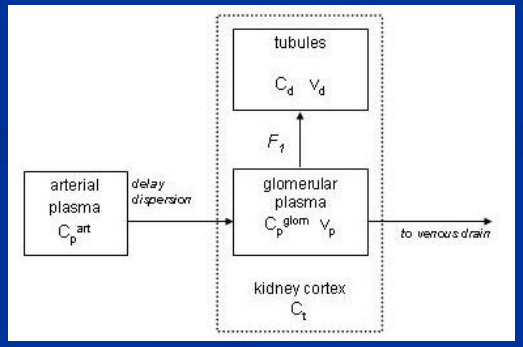
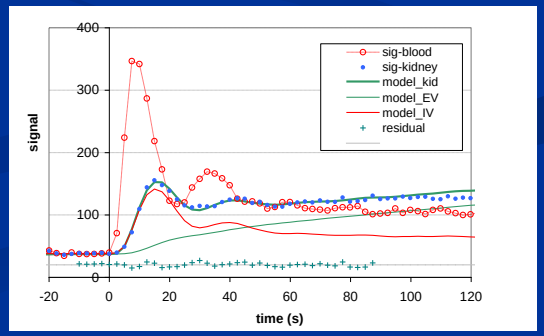
parenchymal ROIs in uptake mode

		MRI mean±sd	instrumental sd	literature normal
filtration (min^{-1})	K^{trans}	0.25±0.05	0.04 (15%)	0.28(a)
blood volume (%)	v_b	34±8	6 (17%)	35 (c)
perfusion ml blood min^{-1} $(100\ ml)^{-1}$	F	219±53	26 (12%)	258(b)
filtration fraction (%)	FF	15.5±2.8	1.2 (8%)	15-20
Mean Arrival Time (s)	MAT	5.9±0.7	0.4 (6%)	6.5 (d)
absolute single kidney volume (ml)	V_{kid}	230±28	-	213
standardised kidney volume (ml)	V_{kid}^*	214±20		213
total GFR (ml min^{-1})	115	27		120

Values in yellow are updated from abstract values (using F from peak of gaussian GIRF, and Hct^{small}=24%)

(a) = $GFR/(2V_{kid}^*)$ (b) using RBF = 1.1 litre min^{-1} (c) from CT (d) Sourbron Invest Radiol 2008

CONCLUSION: our values for four physiological parameters are accurate (and FF and MAT are precise and could be useful)

Summary

- Use uptake phase, parenchymal ROI's and incorporate delay and dispersion in the model
- Filtration and vascular parameters can be estimated with acceptable precision (6-15%)
- Accuracy is good (in agreement with literature).
- Accurate perfusion from peak of gaussian Glomerular Impulse Response Function
- Accurate blood volume using small vessel haematocrit (24%)
- The perfect biomarker! Biologically relevant, precise and accurate
- Total GFR is accurate and could be used clinically to measure single kidney GFR
- This talk: on http://qmri.org
- Matlab GUI by Andy McGovern: http://www.mcgov.co.uk/toftsmodel