

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

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Hypothesis: A recent compartmental model^{1,2} of DCE-MRI can provide precise and accurate measurements of renal filtration, blood flow and blood volume, and hence be reliable enough for clinical studies. Precision would be estimated from repeated measurements; accuracy by comparison with published normal values.

Introduction: A 3-compartment model² fits DCE data with small residuals. Two modes have been described: *uptake mode* (for data up to 90s, when efflux is ignored), and *complete mode* (for longer time-series, when efflux is allowed). Cortical and parenchymal ROI's have been studied.

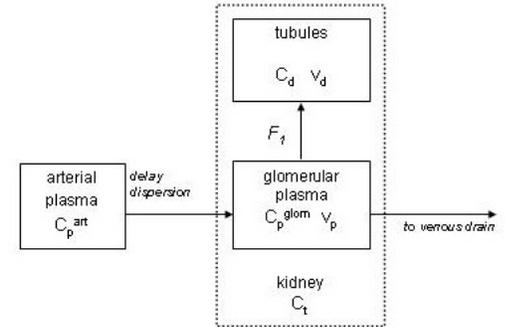
Methods: MRI: 15 normal subjects were imaged before and after injection of 0.05 mmole/kg of Gd-DTPA, on a Siemens 1.5T Avanto imager, using a TIM 32 channel body phased array coil. A spoiled gradient echo 3D sequence had TR=1.6ms, TE=0.6ms, FA=17°. 18 contiguous 7.5mm slices were collected every 2.5s, with in-plane resolution 3.1 x 3.1mm, covering both kidneys. Subjects were imaged a week later, giving a total of 60 normal kidney curves.

Compartmental Modelling: The 3-compartment model^{1,2} was simplified to exclude efflux:

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

$$C_t(t) = v_b(1 - Hct^{small})C_p^{glom} + K^{trans} \int_0^t C_p^{glom}(\tau)d\tau$$

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 for plasma-borne tracer travelling from the aorta to the glomeruli are described by the Glomerular Impulse Response Function (GIRF) $g(t)$. F_1 is the tracer extraction rate per unit volume ($\text{mmole min}^{-1} \text{mL}^{-1}$) from the glomerular plasma by the kidney; $F_1 = K^{trans} C_p^{glom}$; K^{trans} is the transfer constant³ from glomerular plasma to kidney (GFR per unit volume of tissue).

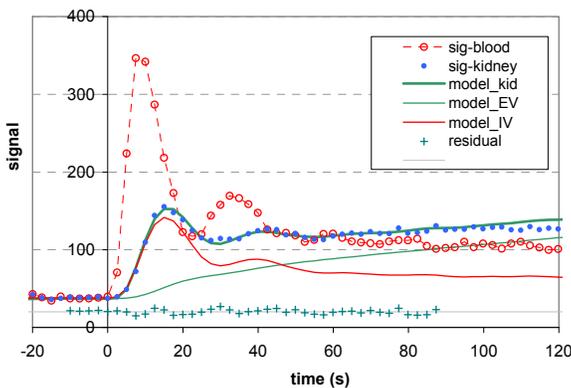


MRI modelling: There were 4 free parameters: v_b , K^{trans} , and 2 delay and dispersion parameters which defined the GIRF. Three GIRF shapes were investigated: instant exponential decay; delayed exponential decay; and delayed gaussian. Blood flow F was estimated from the peak, and also using $F = v_b/MTT$ (MTT =mean transit time). Filtration Fraction $FF = K^{trans}/F$. Perfusion mode (using tissue data up to the post-bolus dip) enabled F and v_b to be estimated with minimal influence of filtration.

MRI analysis: AIF's were found from the descending aorta. Blood $T_{10} = 1.4$ s; parenchyma $T_{10} = 1.2$ s. Relaxivity $r_1 = 4.5 \text{ s}^{-1} \text{mM}^{-1}$. $Hct = 41\%$. Kidney volume was measured from ≈ 8 slices in each kidney. Normal group ($n=15$) mean and sd were found. Instrumental sd was found from the repeats using Bland Altman analysis. Body Surface Area was estimated from $BSA (\text{m}^2) = 0.0235 \text{ Height}(\text{cm})^{0.422} \text{ Weight}(\text{kg})^{0.514}$.⁴ Standardised kidney volumes (for $BSA=1.73\text{m}^2$) were calculated.

Normal single kidney volume V_{kid} was estimated from the published normal value of mass $m=150\text{g}$ as follows: $V_{par} = m/\rho$; $V_{kid} = V_{par}/(1-\alpha v_b)$ (V_{par} =total volume of parenchyma (excluding blood); ρ =parenchymal density=1.03; α =fraction of blood that drains out when kidney is excised and weighed (estimated $\alpha=0.9\pm 0.1$); $v_b=0.35$ (ref⁵). Thus $V_{kid}=213\pm 11$ mL.

Results: Delayed exponential and gaussian GIRF's fitted better (rms residual $\approx 3\text{-}4\%$) than instant exponential; gaussian values are shown in the table. Cortical ROI's gave higher values of filtration, and lower MTT 's, than parenchyma, as expected. However parenchymal v_b (44%) and F were unexpectedly higher than cortical v_b (35%) and F . Perfusion mode gave better fits than uptake mode (residuals $\approx 1\%$ lower); however reproducibility and perfusion parameters were the same.



		MRI normal mean±sd	instrumental sd	literature normal
filtration (min^{-1})	K^{trans}	0.25±0.05	0.04 (15%)	0.28(a)
Mean Transit Time (s)	MTT	5.9±0.7	0.4 (6%)	6.5 ⁶
blood volume (%)	v_b	44±10 (b)	7 (17%)	35%(c) ⁵
blood flow $\text{mL min}^{-1} (100 \text{ mL})^{-1}$	F	495±153 (d)	62 (12%)	258(e,f)
filtration fraction (%)	FF	8.9±1.6	0.7 (8%)	15-20 ⁷
absolute kidney volume (mL)	V_{kid}	230±28	-	213
standardised kidney volume (mL)	V_{kid}^*	214±20	-	213
GFR (mL min^{-1})	GFR	115±27	-	120 ⁷

(a) = $GFR/(2V_{kid}^*)$ (b) right cortical $v_b=35\%$ (c) CT method⁵ (d) right cortical $F = 435 \pm 110$ (e) using total RBF=1.1 L min^{-1} ⁷ (f) cortical $F = 416$ (Case Kid Int 1978;13:236)

Table: analysis of parenchymal ROIs in uptake mode

Figure: uptake mode fit to parenchymal ROI for 90s

Discussion and Conclusions:

- Three renal physiological parameters (filtration, MTT and blood volume) when measured using MRI, have instrumental SD $\approx 6\text{-}17\%$; thus realistic group and individual differences might be reliably detected. Clinical studies would demonstrate sensitivity of these parameters to physiological change.
- The accuracy of the filtration values (K^{trans}) is excellent (see table).
- Mean transit time MTT is precise, unaffected by T_{10} , Hct or r_1 , possibly as sensitive to physiological changes as blood flow, and a good biomarker candidate.
- The accuracy of *parenchymal* blood volume v_b (and hence blood flow F and filtration fraction FF) is disappointing. v_b appears to be too high, giving high F and low FF. Similarly high parenchymal F values from DCE MRI have been reported by Sourbron⁶ (plasma flow = 220; $F = 370$).
- Right *cortical* v_b and F are accurate. Left cortical values showed an inexplicable and significantly higher v_b and F ($p < 1E-8$).
- Possible causes of parenchymal perfusion parameter inaccuracy are naive modelling of the medullary vasculature, or systematic error from assumed T_{10} , FA, Hct or r_1 (a small vessel Hct=30% would give reduced $v_b=37\%$).
- Tubular relaxivity r_1 may be as low as 50% of the assumed in-vitro value⁸ and would increase estimates of K^{trans} but not v_b or F .
- Our measured standardised single kidney volume (214 mL) agrees with an estimate from the published mass (150g) that takes account of the large blood volume; it differs from the value obtained using the naive assumption of unit density (this gives 150 mL).
- Improved movement correction might improve the repeatability.

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