How to best distribute doses in a two-injection dynamic contrast MR renography study?

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Dynamic MR imaging following administration of gadolinium-based contrast agents allows noninvasive estimation of physiological parameters in the kidneys, including glomerular filtration rate (*GFR*). Repeat measurements are often performed before and after pharmacological stimulation. For example, *GFR* reduction after administration of an ACE-inhibitor has been proposed as an improved diagnostic marker of renovascular disease. Based on realistic arterial and renal tissue curves measured in human subjects, we performed Monte Carlo simulations to establish the effect of dose distribution in a dual injection measurement of *GFR*.

METHODS

Data for Monte Carlo modeling were obtained by averaging the signal intensity curves observed in five normal controls and seven patients with renal insufficiency. MRR was performed on a 1.5T Avanto (Siemens, Erlangen, Germany) using phased-array coils and parallel reconstruction. We acquired dynamic, oblique-coronal 3D spoiled gradient echo sequences (Fig 1) with parameters: TR 2.2 ms, TE 0.8 ms, flip angle 12º, 134x256 acquisition matrix, FOV 380 mm, 48 interpolated partitions 2.5 mm thick, 3 sec acquisition time.

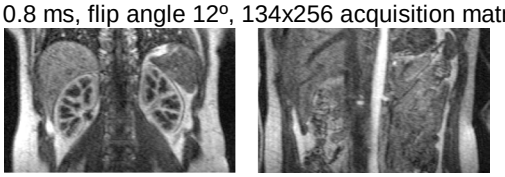


Figure 1

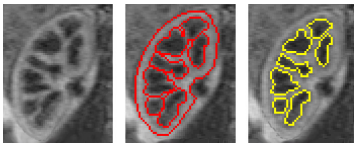


Figure 2

Acquisitions are repeated for 20 min following intravenous injection of d_0 = 4 ml Gd-DTPA (500 mM/L) yielding time points. Semi-automatic image coregistration and segmentation algorithms were used to define ROIs in abdominal aorta, renal cortex and renal medulla (Fig 2). Signal intensities in these ROIs were then converted to Gd-DTPA concentration, based on measured pre-contrast signal intensity S' and T1 relaxation time. An ideal, noise-free arterial input function $A_0(t)$ was obtained by averaging arterial input of our subjects after aligning the time axes to match the time of arterial peaks. For an arbitrary dual injection experiment using doses d_1 and d_2 and separated by inter-injection time delay t_d (Fig. 3), the arterial input is given by $A(t) = (d_1/d_0)A(t)+(d_2/d_0)\,A(t-t_d)$ [1].

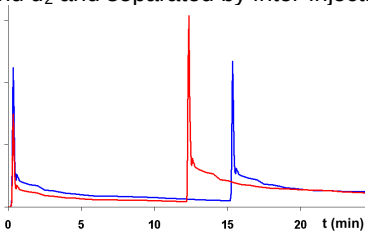


Figure 3

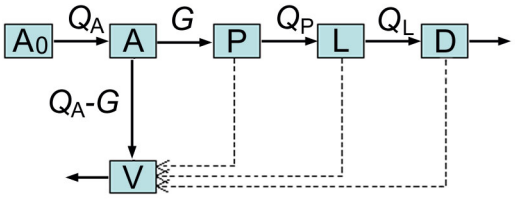


Figure 4

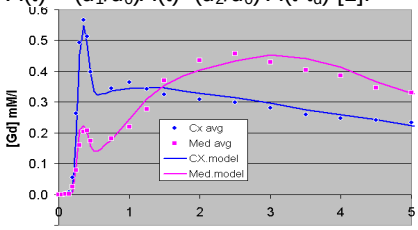
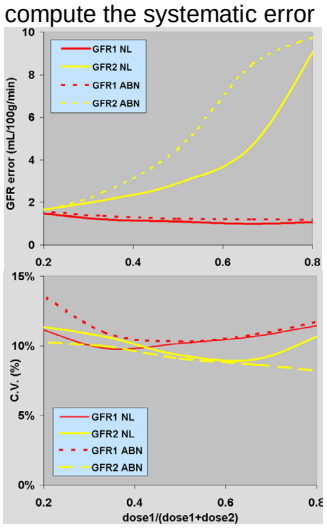


Figure 5

The vascular-nephron model (Fig. 4) is a system of interacting compartments: aorta (A_0), intrarenal arteries (A), veins (V), proximal tubules (P), loops of Henle (L), and distal tubules (D). Parameters include flows Q_A, G=GFR, Q_P, Q_L and tracer-free resorption rates (dashed lines in Fig 4). There was good agreement between observed and model-predicted concentration curves (Fig. 5, model = solid lines, dots = averages for five normal volunteers). Parameter fitting software was implemented in C-language to achieve several hundred Monte Carlo trials per second. For a given dual injection protocol we simulated two models: (a) NL, with realistic normal values of all parameters, and b) ABN, reflecting poor renal function (*GFR* = 30 ml/min). In each Monte Carlo trial we simulated MR data noise at each time point of the dual injection experiment. Noisy curves were then separated into the first and the second data set and subjected to two runs of parameter-fitting algorithm. Statistical distribution of fit results allowed us to compute the systematic error (i.e., the bias) and the precision (measured as the coefficient of variation, C.V.) in GFR_1 and GFR_2.

RESULTS AND DISCUSSION

As long as the total dose d_1+d_2 exceeds 6 ml, both the bias and the precision of GFR_1 and GFR_2 are only weakly dependent on total dose. The error in GFR_2 diminishes from 7 to 4 ml/min as inter-injection delay t_d increases from 10 to 15 min. Results for varying $d_1/(d_1+d_2)$ (shown on the right) assume d_1+d_2 = 12 ml and t_d = 15 min. For all values of $d_1/(d_1+d_2)$, errors in GFR_2 are significantly larger than errors in GFR_1. Reduced GFR_2 accuracy is most likely related to the need to estimate the background signal prior to the second injection. However, within the range $0.2 < d_1/(d_1+d_2) < 0.4$, the systematic error is less than 3 mL/min, which is of the order of 5-10% of measured value. The error increases rapidly if the second dose is significantly lower than the first dose. For $0.3 < d_1/(d_1+d_2) < 0.8$, C.V. is approximately 10% in all cases, i.e. in a clinically acceptable range.



Our results suggest the feasibility of dual injection measurements using MRR. We found d_1 = 0.4 (d_1+d_2) to be near-optimal distribution of the two doses. Moreover, accurate and precise *GFR* measures appear feasible at doses of Gd-DTPA that are several times lower than current standards. Low doses enable functional MRR measurements in conjunction with renal MRA in the same study, a promising strategy for improving the diagnosis of renovascular disease.

References

[1] Bae, Radiology 2003; 227:809–816