A two-compartment model with automatic time interval selection for estimation of GFR using DCE-MRI in cohort of 28 survivors of unilateral Wilms' tumor

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Target Audience: Scientists and clinicians who are interested in assessment of renal function by MRI.

Introduction: Glomerular filtration rate (GFR) is a very important quantitative index of renal function in health and disease. Renal MRI has the potential to quantify GFR serially without exposing patients to ionizing radiation. Several methods are available to estimate GFR using MRI,[1] but a precise and unbiased method to estimate GFR remains to be developed. The purpose of this study is to estimate GFR by dynamic contrast-enhanced (DCE) MRI using a two-compartment model (2C) that disregards tubular outflow and automatically picks the end-of-uptake point (auto2C), and to compare these results with those from the gold standard GFR measurement (^{99m}Tc-DTPA) in long-term survivors of unilateral Wilms' tumor.

Method: 28 long-term survivors of unilateral Wilms' tumor who were successfully given contrast injections participated in this ongoing IRB approved study. All patients underwent nephrectomy as part of their initial therapy and had only a single kidney at the time of the MR exam. A multi-slice T1-weighted 2D FLASH sequence with nonselective saturation recovery preparation (TE/TR=0.98 ms/347 ms, flip angle=8°, matrix=192*192, voxel size= 2.6*2.1*8.0 mm^3) was used for acquiring DCE images on a 1.5T Siemens Avanto scanner. Images were acquired in oblique-coronal planes passing through the aorta and the remaining kidney. Half of the clinical dose (0.05 mmol/kg body weight) of Gd-DTPA contrast agent (CA) was injected in order to avoid failure of the linear relation between CA concentration and signal intensity (SI) at high concentrations. 135 image sets were obtained: 10 before (baseline) and the remaining after contrast injection. A customized signal analysis tool was used for image registration, motion correction, and signal intensity analysis. ROIs were drawn in the suprarenal abdominal aorta and over the single kidney encompassing the parenchyma (Fig. 1). A two gamma variate function was used to fit the arterial input function (AIF) using the SI curves in the aorta. For GFR quantification, we used a 2C model that takes into account both the tracer arterial delay and the bolus dispersion in the glomeruli.[2] However, compared to the referenced model, our model was fitted only for the uptake phase by turning off the tubular outflow because no significant amount of tracer leaves the kidney during the uptake phase.[3] We observed that the uptake phase significantly varied among our patients (Fig. 2a shows the variation in 3 patients from 52 s to 146 s post-aortic) and thus, in our study, the uptake interval was selected automatically for each patient by picking the maximum point on the renal SI curve after the vascular phase (i.e., end-of-uptake point). AIF and compartmental data were fitted using the Trust-Region nonlinear least squares algorithm in Matlab. For parenchymal volume measurement, non-contrast multislice T1-weighted images were semi-automatically segmented using Amira. The parenchymal volume was used to compute the mean MR-GFR of the single kidney as the model outputs the GFR values per volume of renal parenchyma (GFR_V). The mean MR-GFR values were normalized to the body surface area and were correlated with ^{99m}Tc-DTPA GFR values using linear regression and Pearson's correlation coefficient R.

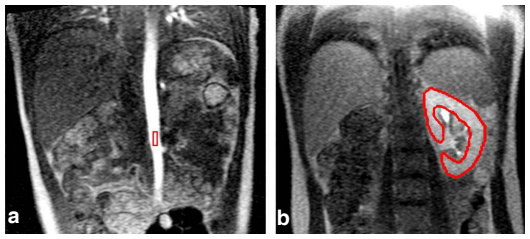

Figure 1: ROIs in (a) aorta and (b) parenchyma in a patient.

Results: The reference ^{99m}Tc-DTPA GFR value [mean±stdev (range)] was 86±14 (61–113) ml/min/1.73 m^2 and mean MR-based GFR_V was 0.30±0.07 (0.15–0.49) min^{-1}/1.73 m^2. Mean parenchymal volume of the single kidney was 241±53 (158–333) ml and mean renal MR-GFR value was 70±17 (40–114) ml/min/1.73 m^2. Fig. 2b & 2c show the AIF fit with the two-gamma variate function and the auto2C model fit for a single patient. The mean uptake interval in our cohort was 86±23 (40–146) s post-aortic. MR-GFR estimates correlated well with the ^{99m}Tc-DTPA (R=0.79, P<0.005) and showed a slope=0.92 (Fig. 2d).

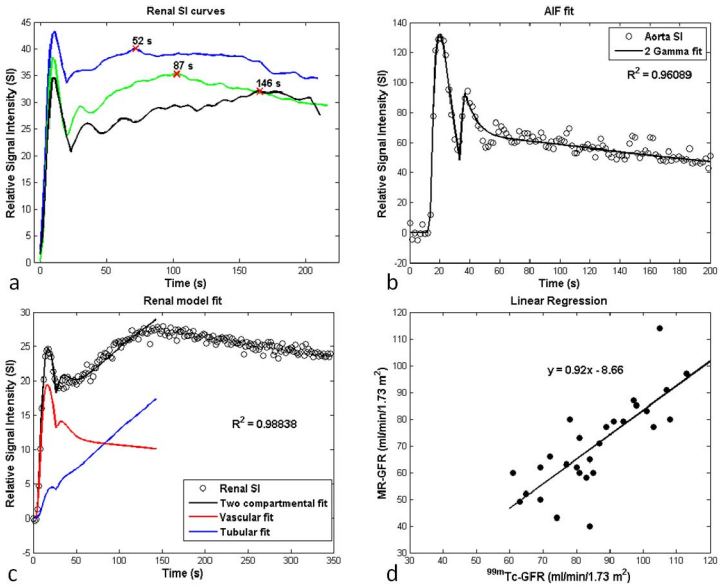

Figure 2: (a) Renal SI curves for 3 patients, (b) AIF fit, (c) auto2C model for one patient, and (d) Linear regression for all patients.

Discussion & Conclusion: DCE-MRI of the kidneys has emerged as a potential measure to quantify GFR. However, GFR quantification using compartmental models involves many challenges such as (a) the number of compartments to model the kidney, (b) modeling AIF accurately, (c) considering with outflow or no-outflow conditions, (d) selection of the fitting interval, (e) fitting of parenchymal or cortical data, etc.[1] Taking tubular outflow into account led to overestimation of GFR likely due to model degeneracy during the efflux phase and uncertainty in the time interval for analysis.[4] In our model, we turned off the outflow and fitted parenchymal data, as cortical data produced lower-quality fits and underestimated GFR due to the complexity in describing the cortical curve.[1] We observed that the uptake interval varied significantly among patients and selecting a fixed interval would under- or overestimate the GFR. Our auto2C model automatically picked the end-of-uptake point, thereby reliably selecting the fitting interval for each patient. Our model produced good fits (R^2>0.95) and the results showed significant correlation (R=0.79, P<0.005) with the reference GFR values.

References: [1] Bokacheva L JMRI 2009, 29:371 [2] Annet L JMRI 2004, 20:843 [3] Patlak CS J Cereb Blood Flow Metab 1983, 3:1 [4] Tofts PS ISMRM 2009; 408.