Renal tracer kinetics with a reabsorption correction

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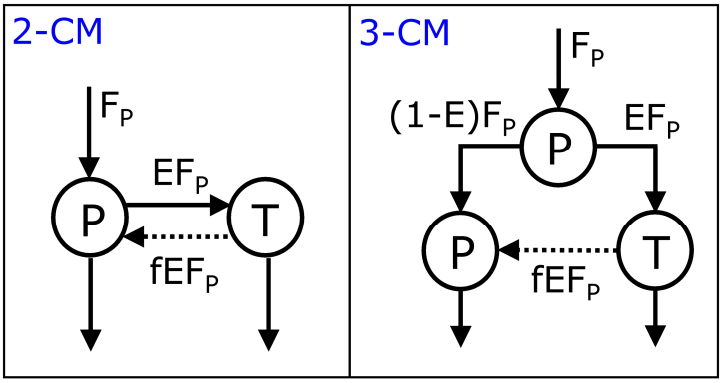

Figure 1. The two-compartment (2-CM, left) and three-compartment (3-CM, right) models with reabsorption correction. Plasma (P) and Tubular (T) spaces exchange flows through channels that contain tracer (full line) and channels that only contain systemic substances (dotted line). In the 3-CM, the plasma space is divided in glomerular (top) and peritubular (bottom left) capillaries. Symbols near the arrows denote the flow carried by the corresponding channel. The total flow into the plasma compartment is denoted with F_P, the extraction fraction with E, and the reabsorption fraction with f.

Mean (stddev)	F_P (ml/100ml/min)	T_P (s)	T_T (s)	E (%)	f (%)	V_P (ml/100ml)	V_T (ml/100ml)
2-CM	265 (76)	3.8 (0.9)	115 (70)	**12 (3.3)**	**65 (11)**	**17 (2.4)**	**18 (7.6)**
3-CM	191 (53)	5.3 (1.1)	113 (67)	16 (3.9)	**71 (10)**	**16 (2.1)**	**14 (4.7)**

Table 1. Mean (stddev) of the fitted model parameters for all 15 volunteers. Parameters in black are derived by fitting the kidney curve alone, parameters in **blue** by fitting the kidney curve and the VOF simultaneously. The volumes V_P and V_T are combinations of the 5 independent parameters $\{F_P, T_P, T_T, E, f\}$.

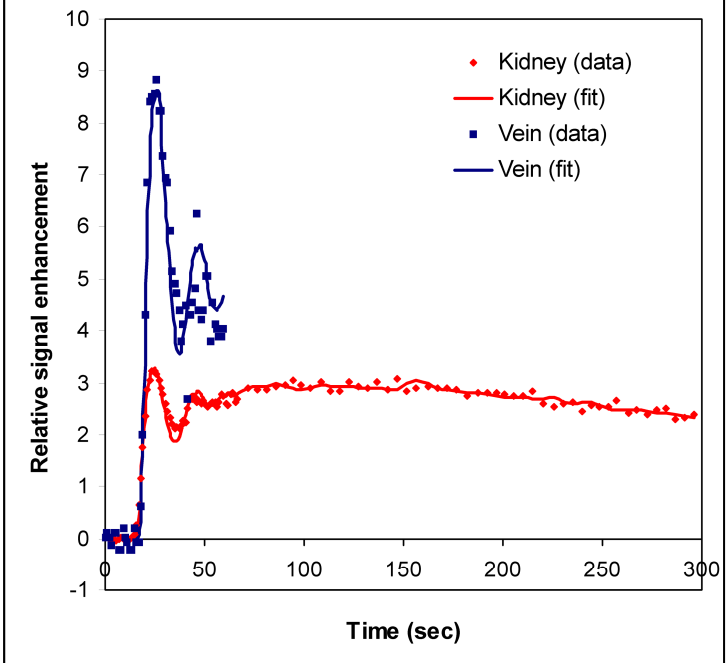

Figure 2 An example of the simultaneous fit of kidney curve and venous outflow function to the three-compartment model.

INTRODUCTION Current tracer kinetic models for the analysis of bolus-tracking data in the kidney do not effectively account for the effect of reabsorption of the fluid filtered in the glomerular capillaries [1,2,3]. The flow of tracer-free fluid is either not included in the model [1,2], or it is assumed to leave the tubular space directly to the exterior space [3]. This leads to an inaccurate description of the microscopic flow processes in the kidney, and unphysical values for the reabsorption fraction [3]. The aim of this study is to propose two alternative models of reabsorption, to analyse their limitations and potential from an analytical perspective, and provide a first assessment of the effect of this reabsorption correction using data acquired in healthy kidneys.

METHODS Dynamic contrast enhanced MRI obtained at 1.5T in 15 healthy young male volunteers were analysed retrospectively [4]. Four slices (1 axial, 3 coronal) were acquired every 1.1s for 5 min, using a 2D saturation-recovery Turbo-Flash sequence (matrix 112x192, TE 0.98ms, TI 148ms, FA 12°, slice thickness 8mm, pixel size 3.35 x 2.34 mm^2). 7ml Gd-BOPTA (Multihance, Bracco-Altana) was injected at a rate of 4ml/s. Data were post-processed using the software PMI 0.3 written in-house in IDL 6.4 (ITT Visual Information Solutions). Regions-of-interest were drawn manually in the aorta and the renal vein on the axial slice to measure the Arterial Input Function (AIF) and the Venous Outflow Function (VOF), and on the kidney in the middle coronal slice. Only the first 60s of the VOF were used due to difficulties in measuring the VOF during breathing. Tracer concentrations were approximated by the relative signal enhancement $(S-S_0)/S_0$ and fitted to the 2-compartment (2-CM) and 3-compartment (3-CM) models in figure 2. The excretory phase of the models was weighted with a factor 0.5 to correct for the difference in Gd-BOPTA relaxivity between plasma and filtrate in healthy kidneys.

RESULTS Exploratory measurements demonstrated that the 3-CM produced nearly equal mean transit times (MTT) for both plasma compartments. Hence the constraint that both MTTs are equal was built into the 3-CM, so that both models are fully defined by 5 independent parameters: the plasma flow (F_P), the plasma MTT (T_P), the MTT *of the tracer* in the tubuli (T_T), the extraction fraction (E) and the reabsorption fraction (f). The solution of the model equations shows that a model-fit to a kidney curve alone allows to determine 4 free parameters: both 2-CM and 3-CM produce the parameters F_P, T_P and T_T; the 4th parameter is the extraction fraction E for the 3-CM, but for the 2-CM it is the combined parameter E/(1+fE). Hence the 2-CM does not allow for a measurement of E, and neither model produces a value for f. These limitations can be overcome by using the information provided by the VOF. When kidney curve and VOF are fitted simultaneously, the full set of 5 independent model parameters $\{F_P, T_P, T_T, E, f\}$ can be determined. These values can be combined to determine the tubular volume V_T and the plasma volume V_P as well. The models were first fitted to the 15 kidney curves alone (Table 1, black values). They were then fitted to kidney curves and VOFs simultaneously to determine the remaining parameters (Table 1, blue values). Figure 2 shows an example of a simultaneous fit to both curves. Both models fitted the data equally well: $\chi^2 = 0.25\ (0.10)$ % for 2-CM and $\chi^2 = 0.24\ (0.10)$ % for 3-CM.

CONCLUSION The analysis shows that a 2-compartment model without reabsorption [1,2] satisfies the same model equation as the 2-CM, but underestimates the extraction fraction by a factor 1+fE. Both corrected models fit the data equally wel, but only the 3-CM produces a mean F_P inside the range of typical gold-standard values [5]. The 3-CM describes renal physiology more correctly and produces a measurement of E (or the glomerular filtration rate) in the most straightforward manner from a fit to a kidney curve alone. Both models allow to measure two additional parameters (f and V_T) that cannot be determined separately with existing methods [1,2,3]. The measured reabsorption fractions agree with typical values for the combined reabsorption in the proximal tubuli and the loop of Henle [3]. We conclude that the 3-CM is the most attractive approach to reabsorption correction from a practical and a conceptual perspective. Combined with an additional measurement of the VOF, it allows for a more complete characterization of renal function than existing models.

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