A Comparison of Deconvolution and the Patlak-Rutland Plot in Renography Analysis

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Deconvolution and the Patlak-Rutland plot are two of the most commonly used methods for analyzing dynamic radionuclide renography. Both methods allow estimation of absolute and relative renal uptake of radiopharmaceutical and of its rate of transit through the kidney. **Methods:** A theoretical comparison of uptake assessment by both techniques is made and a mathematical derivation of the relationship between mean transit time (MTT) and renal outflow efficiency (ROE) is presented. The validity of these theoretical findings was tested in a series of 120 renograms obtained using ^{99m}Tc-mercaptoacetyltriglycine (MAG3). **Results:** The estimates of renal uptake obtained are theoretically equivalent. The renogram measurements confirmed this, because there was no significant systematic difference in relative counts obtained by the two methods. Absolute counts were significantly higher for the deconvolution measurements, but only by 2.0%. The SDs of the differences between the two techniques, expressed as a percentage of the mean, were 1.7% and 5.4% for relative and absolute counts, respectively. There was an inverse monotonic relationship between MTT and ROE. ROE evaluated at a particular time was shown to depend on absolute renal function. Measured values of MTT and ROE were consistent with the theoretical prediction. **Conclusion:** The two approaches to renogram analysis provide consistent parameters for both uptake and transit evaluation.

Key Words: renography analysis; deconvolution; Patlak-Rutland plot

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Gamma camera renography has been used widely for the assessment of renal function over the last 20 years (*1*). Many methods have been used to derive quantitative parameters from the measurements (*2–5*). The uptake of activity in the kidney before the minimum transit time of the radiopharmaceutical is taken as a measure of renal function. Both relative and absolute uptake may be calculated, the latter by relating renal activity to the injected dose (*6*). Measures of the rate of transit of radiopharmaceuticals through the kidney, such as the peak time (*7*), mean transit time (MTT) (*8*) or renal outflow efficiency (ROE) (*9*), may also be calculated. These parameters are useful in the evaluation of upper urinary tract obstruction, in which they have been shown to improve diagnostic accuracy in patients with impaired renal function (*9*), and in detecting renovascular hypertension using angiotensin-converting enzyme inhibitor renography (*7*).

Two of the most commonly used approaches to analysis are deconvolution (*2*) and the Patlak-Rutland plot (*4*). Both methods attempt to use information on the time variation of the input to the kidney to obtain functional parameters that are independent of the shape of this curve. Both methods also provide a means of subtraction of intrarenal vascular activity and therefore of estimation of the true renal uptake. This article will compare the two techniques for the calculation of renal uptake in theory and then in practice in a series of patients with a variety of renal function. Both techniques also allow assessment of a parameter of renal transit. Deconvolution measures the MTT, whereas the Patlak-Rutland plot principle leads naturally to the concept of a zero output curve and hence to the ROE (*9*). A theoretical relationship between MTT and ROE is derived, and these two parameters are also compared in the same series of patients.

MATERIALS AND METHODS

Theoretical Comparison of Uptake

Both deconvolution and Patlak-Rutland plot approaches to the assessment of renal uptake are based on the assumption that up to a given time after injection (t_1), corresponding to the minimum transit time, there is no output of activity from the renal region of interest (ROI). The activity in the region, R(t), may then be described as:

$$R(t) = a\int_0^t I(\tau)\,d\tau + bI(t) + cE(t) \quad \text{for} \quad t < t_1, \qquad \text{Eq. 1}$$

where I(t) is the time-activity curve in blood; E(t) the time-activity curve for extrarenal contribution; and a, b and c are constants. E(t) is made up of both vascular and extravascular components. Constant a is the fraction of vascular activity cleared by the kidney per unit time. It is proportional to the effective perfusion of the kidney, the product of perfusion and extraction efficiency for the radiopharmaceutical and provides a measure of renal function.

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The extrarenal contribution is subtracted by estimating cE(t) from the count variation over a background ROI (*8*). This defines the extrarenal background subtracted renogram $R_1(t)$ as:

$$R_1(t) = a\int_0^t I(\tau)d\tau + bI(\tau) \quad \text{for} \quad t < t_1. \qquad \text{Eq. 2}$$

Constant b describes the contribution from the vascular content of the kidney itself. The term $a\int_0^t I(\tau)d\tau$ describes the actual renal uptake curve K(t). It is usual to estimate I(t) from the cardiac (*4*) or background-subtracted cardiac (*10*) curve.

In the Patlak-Rutland plot analysis, Equation 2 is reduced to linear form by division by I(t):

$$R_1(t)/I(t) = a\int_0^t I(\tau)d\tau/I(t) + b. \qquad \text{Eq. 3}$$

A plot of $R_1(t)/I(t)$ against $\int_0^t I(\tau)d\tau/I(t)$ gives a straight line allowing gradient a and intercept b to be estimated by linear regression. The actual kidney uptake curve K(t) up to the minimum transit time can then be estimated as:

$$K(t) = a\int_0^t I(\tau)d\tau \quad \text{for} \quad t < t_1. \qquad \text{Eq. 4}$$

The process of solving Equation 2 for constant a by deconvolution can be understood by considering the Laplace transformation of the equation:

$$R_1(s) = aI(s)/s + bI(s). \qquad \text{Eq. 5}$$

Deconvolution of R_1 with respect to I involves division of the above equation by $I_{(s)}$, i.e.:

$$R_1(s)/I(s) = a/s + b. \qquad \text{Eq. 6}$$

The inverse Laplace transform of Equation 6 gives:

$$H(t) = a + b\delta(0) \quad \text{for} \quad t < t_1, \qquad \text{Eq. 7}$$

where H(t) is the renal retention function, the response of the kidney to a bolus input and δ (0) is the delta function at time zero. The value of constant a can be found from the average value of the retention function after the initial spike due to the delta function. The true kidney curve can then be found by convolution of a with I(t), giving the same equation as for the Patlak-Rutland plot, i.e., Equation 4.

This argument shows that the subtraction of vascular background using both approaches is, in principle, very similar and, provided other aspects of the analysis are the same, the assessment of renal function should yield similar results. The subsequent experimental comparison aims to test this hypothesis.

Theoretical Relationship Between Mean Transit Time and Renal Outflow Efficiency

The renal uptake curve K(t) formed as a result of convolution between an input function I(t) and renal retention function H(t) with a single transit time T is considered, where: H(t) = a for $0 < t < T$, and H(t) = 0 for $t > T$. The resultant renal uptake curve is given by:

$$K(t) = a\int_0^t I(\tau)\,d\tau \quad \text{for} \quad 0 < t < T,$$

$$K(t) = a\int_{t-T}^t I(\tau)\,d\tau \quad \text{for} \quad t < T. \qquad \text{Eq. 8}$$

The zero output curve up to time t is given by:

$$Z(t) = a\int_0^t I(\tau)d\tau. \qquad \text{Eq. 9}$$

Thus, the ROE, which is defined by the amount of activity that has passed through the kidney at time t as a percentage of that taken up, is given by:

$$\begin{aligned} ROE(t) &= 100\left[a\int_0^t I(\tau)d\tau - a\int_{t-T}^t I(\tau)d\tau\right]\Big/\left[a\int_0^t I(\tau)d\tau\right] \\ &= 100\left[\int_0^{t-T} I(\tau)d\tau\right]\Big/\int_0^t I(\tau)d\tau. \end{aligned} \qquad \text{Eq. 10}$$

This assumes that the time of evaluation of ROE is greater than or equal to the transit time t.

The theoretical ROE at a time of 18 min was evaluated for MTT varying between 2 and 18 min using equation 10. Realistic input functions, I(t), were derived from background-subtracted cardiac curves obtained in clinical mercaptoacetyltriglycine (MAG3) studies (*10*). Two extreme situations were considered using subjects with normal and very poor renal function, as judged by their glomerular filtration rate. The background-subtracted cardiac curves were fitted to a triple exponential (*11*) using log linear regression:

$$A\exp(-a_1t) + B\exp(-a_2t) + C\exp(-a_3t),$$

where A + B + C = 1. The value of the parameters used are shown in Table 1.

Data Acquisition and Analysis

A series of 120 patients (age range 1–95 y) referred for routine renography were studied. Patients were hydrated before an injection of ^{99m}Tc-labeled MAG3 (80 MBq in adults scaled by weight; in children, a minimum of 20 MBq). For most patients, the injection was carried out with the patient in a seated position, with the gamma camera viewing the kidneys posteriorly. Very young children and patients who were ill were imaged in the supine position. When indicated, a diuretic was given 8 min after injection. Digital acquisition of 100 frames of 12-s duration was carried out and the data transferred to a Link MAPS 10000 computer (Link Medical, Marlow, UK), with which the analysis was performed.

Regions were drawn manually covering the right and left kidneys, a background area between the upper poles of the kidneys, and the heart. Time-activity curves were then created and the renal curves smoothed by a variable amount, depending on the maximum count (*11*). The smoothing protocol used n passes of a (1–2-1) filter,

TABLE 1
Parameters of Triexponential Function* Representing Input Function to Kidney in MAG3 Renography for Cases of Normal and Poor Renal Function

Renal function	A	B	C	a_1 (min^{-1})	a_2 (min^{-1})	a_3 (min^{-1})
Normal	0.680	0.206	0.113	4.79	0.491	0.120
Poor	0.474	0.296	0.230	3.73	0.354	0.016

*$A\exp(-a_1t) + B\exp(-a_2t) + C\exp(-a_3t)$.
MAG3 = mercaptoacetyltriglycine.
Values were derived from background-subtracted cardiac curves for two subjects with normal and very poor overall renal function.

subject to a minimum of two:

$$n = (12 - c^{1/2}/15), \quad \text{Eq. 11}$$

where c is the count per frame in the kidney curve at 2 min. Extra organ background was subtracted from both renal and cardiac curves as described previously (*8,10*). The background curve was corrected for the relative areas of the ROIs and by an additional factor to allow for the fact that the extrarenal background tissue did not extend the full thickness of the patient, whereas tissue of the background region did. These factors (0.87 for the right kidney, 0.79 for the left kidney and 0.57 for the heart) had been derived for imaging with ^{123}I-hippuran but are assumed to apply to other radiopharmaceuticals, because they principally depend on the relative thickness of the kidney, compared with the thickness of the patient. The factors were derived in adult patients and were found to over-subtract in children. For patients younger than 16 y, the factors were reduced according to age, A, using the following empirical rule:

$$f_c = 0.5 + (f_a - 0.5)\,A/16 \quad \text{for} \quad A<16, \quad \text{Eq. 12}$$

where f_a and f_c are the factors for adults and children, respectively. Background subtraction using this regime has been validated for diethylenetriamine pentaacetic acid (DTPA), by comparing the percentage uptake at 2 min with glomerular filtration rate. The resulting regression curve passed close to the origin, indicating the accuracy of the subtraction technique (*12*). The peak time of the cardiac curve was determined automatically and taken as zero time for all curves.

The data were then analyzed with deconvolution and the Patlak-Rutland plot. Deconvolution was carried out with the matrix method, using a background-subtracted cardiac curve as the input function. The plateau (P) of the retention function was first calculated from the mean value of the curve between 1.2 and 2.0 min. A more robust plateau value (P_1) was then obtained by extending the calculation until time T_p, when the retention function first fell below 0.85 P. Intrarenal vascular background was subtracted by back extrapolation of the plateau value to zero time and replacement of the retention function values before T_p with the plateau level P_1. The corrected retention function was then reconvolved and renal uptake assessed by integrating the curve between 1.2 and 2.0 min.

The Patlak-Rutland plot analysis was applied to the same extrarenal background-subtracted renogram curve. The plot was fitted to a straight line between 1.2 min and T_p and the true renal uptake curve with intrarenal vascular activity was subtracted and calculated as described in the theory section. The renal uptake between 1.2 and 2.0 min was calculated from this curve.

The MTT was calculated from the ratio of area to plateau height of the retention function. The ROE at 18 min was calculated by applying Equation 10 to the renal curve corrected for intravascular background using the Patlak-Rutland plot method. The ROE was calculated at 18 min rather than at 20 min, the total acquisition time, to allow for the fact that setting zero time to the cardiac peak meant that the duration of the processed curves was often less than 20 min.

Relative and absolute renal uptakes derived by the two techniques were compared with systematic and random differences, using the paired *t* test and the Bland-Altman method (*13*), respectively. The variation of ROE with MTT was assessed qualitatively with a scatter plot. The pairs of values were compared with theory by superimposing on the plot the curves representing the theoretical nonlinear relationship between them for normal and poor renal function.

RESULTS

The comparison of relative renal function of the right kidney between the two techniques is shown in Figure 1. There was no systematic difference between the two values, and the random variation showed an SD of 0.85 percentage points, i.e., 1.7%, when expressed relative to the mean. The comparison between the true kidney counts summed between 1.2 and 2.0 min for the two techniques is shown in Figure 2. There was a very small systematic difference between the two assessments, the Patlak-Rutland plot yielding values that were 2% lower ($P = 0.002$). The SD of the difference as a percentage of the mean was 5.4%.

The comparison between MTT and ROE is shown in Figure 3. The theoretical curves, which were derived assuming the input functions detailed in Table 1, show the significant differences in ROE values that can occur for a given MTT with different overall renal function. The correspondence of measured ROE and MTT values generally fell within the extreme limits defined by the theory, illustrating its validity. Kidneys with MTT below 5 min tended to have ROE values close to the theoretical curve obtained using normal renal function, whereas higher MTT values between 10 and 15 min were generally closer to the poor function curve. This correspondence would be expected in most patients, given that extended transit times are usually associated with poorer function. However, it would not be anticipated that this trend would be universal, because the relationship between MTT and ROE is measured for individual kidneys, and overall function applies to the combined effect of both kidneys. In addition, there are errors on measuring both MTT and ROE. These are increased in situations of slow transit and explain the breakdown in the relationship between MTT and ROE for MTT values greater than approximately 15 min. The theoretical relationship is based on the assumption of a single transit time, whereas, in practice, there is a spectrum of transit times. This means that for slow transit, the maximum transit time may be greater than the total acquisition time, causing the MTT to be underestimated as a result of the retention function being incomplete. The precision of the ROE is also likely to be poor in cases of slow transit, because errors due to extrapolation of the cumulative cardiac curve, which is based on normalization to the kidney curve during the first few minutes of acquisition, will be most marked.

DISCUSSION

Deconvolution and the Patlak-Rutland plot have been widely used for analysis of renography, each enabling the derivation of renal uptake corrected for vascular background contribution. In this article, we have shown that the two methods for uptake measurement are theoretically equivalent and have validated this in practice in a series of 120

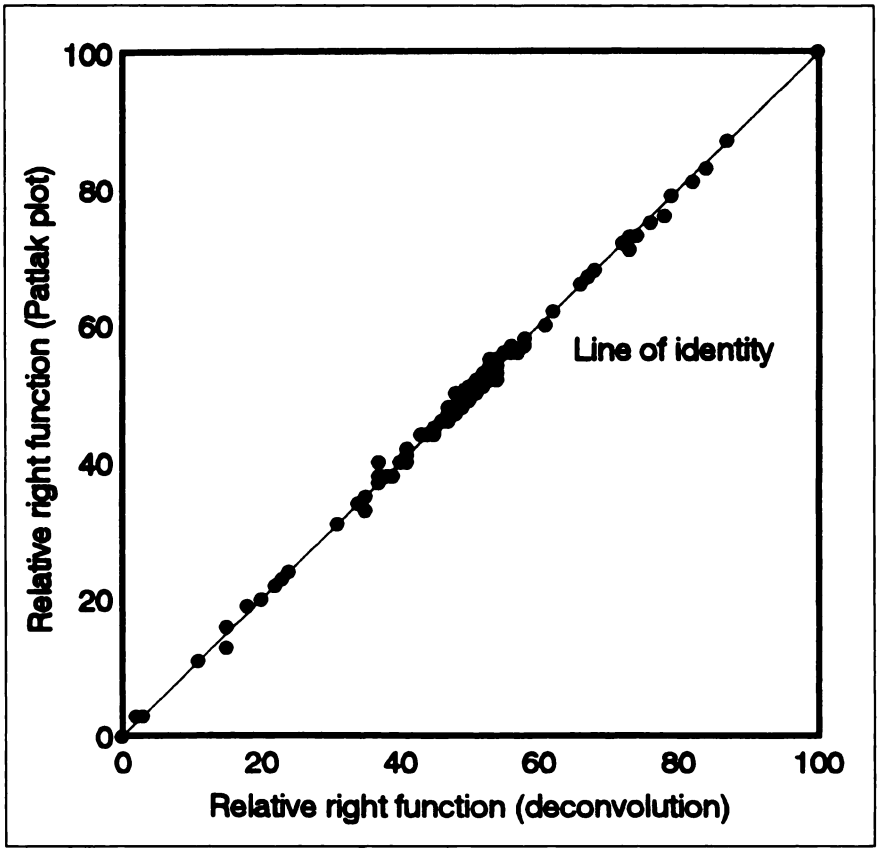

FIGURE 1. Correlation between relative renal function of right kidney assessed from MAG3 renography analyzed by deconvolution and Patlak-Rutland plot.

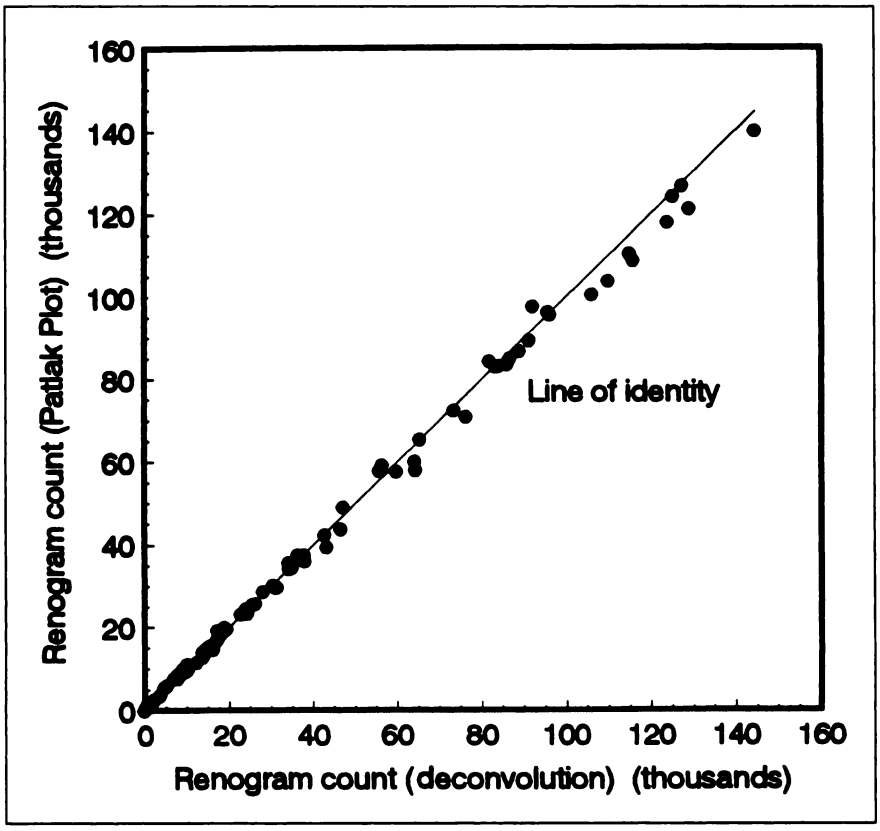

FIGURE 2. Correlation between renal uptake counts summed from 1.2 to 2.0 min for MAG3 renography by deconvolution analysis and Patlak-Rutland plot.

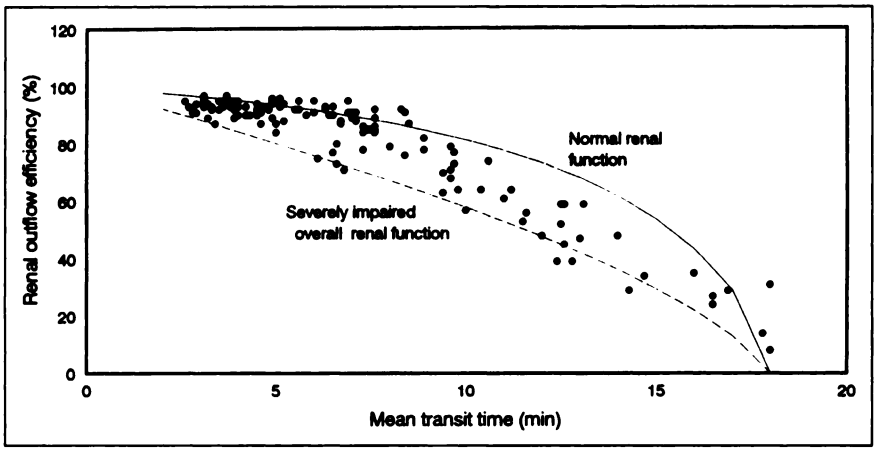

FIGURE 3. Correlation between MTT and ROE for MAG3 renography. Theoretical relationships for normal (solid line) and severely impaired overall renal function (dotted line) are also shown.

renograms that cover a wide variety of ages and both relative and absolute renal function.

Deconvolution also provides parameters of renal transit, such as MTT, that are independent of the input function. However, the use of deconvolution analysis depends on the assumption of time invariance of the spectrum of transit times through the kidney. The ROE parameter has been suggested as a useful alternative to MTT, but this condition is not fulfilled. This occurs, for example, when a diuretic is administered during the investigation. The ROE by comparison is model independent, which means it has the flexibility to be able to quantify the response of the diuretic. However, it has been shown in simulation studies (*11*) that the MTT is a relatively robust parameter, even in the presence of varying transit times, and the use of this approximation is helped by having a fixed time for the administration of a diuretic, as was the case in this study. Moreover, ROE does have the disadvantage of being dependent to some degree on the input function.

CONCLUSION

This study demonstrated the equivalence of deconvolution and the Patlak-Rutland plot in assessing renal uptake function. MTT and ROE are well correlated, which suggests that both are useful in quantifying transit. However, each parameter is subject to its own limitations: MTT to its requirement of time invariance and ROE to its dependence on overall renal function. These factors should be kept in mind in the clinical interpretation of the values obtained.

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