A comparison of deconvolution and the Rutland-Patlak plot in parenchymal renal uptake rate

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ABSTRACT

Introduction: Deconvolution and the Rutland-Patlak (R-P) 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. Materials and Methods: Seventeen patients (32 kidneys) were referred for further evaluation by renal scanning. All patients were positioned supine with their backs to the scintillation gamma camera, so that the kidneys and the heart are both in the field of view. Approximately 5-7 mCi of $^{99m}$Tc-DTPA (diethylenetriamine penta-acetic acid) in about 0.5 ml of saline is injected intravenously and sequential 20 s frames were acquired, the study on each patient lasts for approximately 20 min. The time-activity curves of the parenchymal region of interest of each kidney, as well as the heart were obtained for analysis. The data were then analyzed with deconvolution and the R-P plot. Results: A strong positive association ($n = 32; r = 0.83; R^2 = 0.68$) was found between the values that obtained by applying the two methods. Bland-Altman statistical analysis demonstrated that ninety seven percent of the values in the study (31 cases from 32 cases, 97% of the cases) were within limits of agreement (mean ± 1.96 standard deviation). Conclusion: We believe that R-P analysis method is expected to be more reproducible than iterative deconvolution method, because the deconvolution technique (the iterative method) relies heavily on the accuracy of the first point analyzed, as any errors are carried forward into the calculations of all the subsequent points, whereas R-P technique is based on an initial analysis of the data by means of the R-P plot, and it can be considered as an alternative technique to find and calculate the renal uptake rate.

Keywords: Iterative deconvolution, renal uptake, Rutland-Patlak plot, renogram, renal retention function

INTRODUCTION

Deconvolution and the Rutland-Patlak (R-P) 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. Gamma camera renography has been widely used for the assessment of renal function over the last 20 years. Many methods have been used to derive quantitative parameters from the measurements. 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. Measures of the rate of transit of radiopharmaceuticals through the kidney, such as the peak time, mean transit time (MTT) or renal outflow efficiency (ROE), may also be calculated. These parameters are useful in the evaluation of upper urinary tract obstruction, in which they have shown improvement to diagnostic accuracy in patients with impaired renal function, and in detecting renovascular hypertension using angio-tension-converting enzyme inhibitor renography. Two of the most commonly used approaches to analysis are deconvolution and the R-P plot. 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 the renogram. Both methods also provide a means of subtraction of intrarenal vascular activity and therefore, of estimation of the true renal uptake. Deconvolution is widely used and considered as the gold standard for the estimation of renal transit in conditions in which the transit time is assumed to be prolonged, such as renovascular disease, transplant rejection, and obstructive uropathy. Theoretically, at least, using the renogram as the output function and the plasma disappearance curve as the input function, the spectrum of intra-renal transit times can be determined exactly. In practice, there are many factors which raise questions about the validity of this approach. One of
these, probably the most important, is the relationship between
the spectrum of intrarenal transit times and the duration of data
acquisition. It is mathematically obvious that deconvolution can
only be applied correctly if the maximal transit time is shorter
than the duration of data acquisition. Unfortunately, based on
a renogram, one cannot tell whether the maximal transit time
is longer or shorter than the acquisition time.\cite{29} Deconvolution
analysis has been a useful technique for analyzing organ function
in nuclear medicine\cite{10,20,21} for a considerable time. There are three
established techniques plus one more recent approach.\cite{15} The
three main methods are iterative deconvolution (also known as
matrix inversion), Laplace transforms and Fourier transforms.\cite{22}
The iterative deconvolution analysis has been previously applied
by many authors\cite{10,20,21,24,25} in nuclear medicine investigations. The
deconvolution technique has been extensively and most widely
applied to renal studies.\cite{10,20,21,24} Deconvolution is a mathematical
technique, which overcomes the influence of the tracer input curve
on the renogram. The result of deconvoluting the renogram yields
a function termed the “retention function,” which represents the
form of the renogram that would be obtained if an injection is
given directly into the renal artery. An important advantage of the
retention function and R-P plot have physiological significance, unlike those derived from the renogram such as slope of the second phase, time to peak, and so on. This is, because the renogram is a complex curve which combines both renal and extra-renal factors. Measures of the rate of transit of radiopharmaceuticals through the kidney, such as the peak time,\cite{9} MTT\cite{10} or ROE\cite{15} 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,\cite{13} and in detecting renovascular hypertension using angio-tension-converting enzyme inhibitor renography.\cite{26} The aim of the present study was to compare between the values of the renal uptake rate obtained by two methods, R-P plot (multiple time graphical analysis method)\cite{23,31} and the iterative deconvolution (matrix inversion) using $^{99m}$Tc-DTPA (diethyliminetramine penta-acetic acid). To our knowledge, this research is the first study that compared the values of renal uptake rate applying these two methods using $^{99m}$Tc-DTPA.

THEORY

Theory and derivation of the retention function

In a renogram study, the renal curve ($R(\beta)$), is considered to be
a convolution of the input function (blood curve), which will
be called $B(\beta)$, and the renal retention function (also known as
the impulse response function), which will be called $H(\beta)$. The
retention function represents the curve that would be obtained
if a spike bolus of tracer were delivered at one point in time
into the renal artery. The shape of $H(\beta)$ may be analyzed to
produce information about the function of the kidney being
studied, and one of the most frequently used parameters is the
MTT. The renogram curve, $R(\beta)$, after corrections for blood and
tissue background, is a convolution of the input function from
the blood to the kidney, $I(\beta)$, and the retention function of the
kidney, $H(\beta)$. The main assumption made in this approach is
that the kidney can be modeled as a linear, stationary system.\cite{10,20} In
practice, the linearity of the system is generally maintained, but
stationarity may often be violated.\cite{16} The technique adopted
in this study is that of discrete deconvolution using the matrix
algorithm.\cite{22} This algorithm has been applied previously in
renal deconvolution.\cite{31,26} In this method, the linear matrix
$H$ is evaluated in a successive manner, starting with $H(1)$ and
working through to the final element $H(n)$. Thus, the value of
the retention function in the $k$th interval is given by:

$$H(i) = \frac{1}{(l-1) \Delta t} \left[ \sum_{j=1}^{l} (i-j+1) \cdot H(j) \right],$$

where $\Delta t$ is the sampling interval which is taken to be 20 s in
this study, $R$ and $I$ are obtained by selecting regions of interest over
the kidney and over the heart, respectively, and creating time-activity
curves for the duration of the study. Before evaluating $H$ from
Eq. 1, it is necessary to reduce the effect of statistical variations
inherent in $R$ and $I$. This is achieved by applying once a 1:2:1 linear
non-stationary smooth with appropriate end point constraints to
both kidneys, and input curves since this has been shown to be
an appropriate degree of data filtering in this study.\cite{38}

Principles of Gjedde-Patlak analysis

The original idea of Patlak and Blasberg was to create a model
independent graphical analysis method: Whatever the tracer is
facing in the tissue, there must be at least one irreversible reaction
or transport step, where the tracer or its labeled product cannot
escape.\cite{39} It is assumed that all the reversible compartments must
be in equilibrium with plasma, i.e. the ratio of the concentrations of
tracer in plasma and in reversible tissue compartments must
remain stable. In these circumstances only the accumulation of
tracer in irreversible compartments is affecting the apparent
distribution volume. In practice, this can happen only after
the initial sharp concentration changes when the plasma curve
descends slow enough for tissue compartments to follow.\cite{30} When
the steady state is achieved, the Gjedde-Patlak plot becomes linear.
The slope of the linear phase represents the net transfer rate
$K$ (influx constant). To make it simple, $K$ represents the amount of
accumulated tracer in the kidney to the amount of tracer that has
been available in plasma.\cite{40} The $y$-axis of plot contains apparent
distribution volumes, that is the ratio of activities of tracer in the
kidney and in plasma. On $x$-axis is normalized plasma integral,
that is, the ratio of the integral of plasma activity and the plasma
activity.\cite{22,23,36} The Patlak plot is given by the expression:

$$\frac{C_{\text{plasma}}(\theta)}{C_{\text{plasma}}(\theta)} = \frac{K}{2} \int_{0}^{\theta} \frac{1}{C_{\text{plasma}}(\theta)} \, dt + 1.$$  

(2)

This means that the measured kidney activity is divided by plasma
activity, and plotted at a “normalized time” (integral of input curve
from injection divided by instantaneous plasma activity).\cite{17} For
systems with irreversible compartments, this plot will result in a
straight line after sufficient equilibration time [Figure 1]. The slope
and the intercept must be interpreted according to the underlying compartment model. For the $^{99m}$Tc-DTPA, the slope represents the kidney uptake rate, while the intercept $V$ (as appeared in the equation on the previous page) or $F$, which is due to the blood within the organ (the blood background subtraction factor). The value of $F$ will be equal to the ratio of volumes of the blood activity in the organ to the blood contributing to the blood curve.$^{23}$ For every scintigraphic examination, the renal uptake rate of $^{99m}$Tc-DTPA was calculated twice, applying the two methods R-P plot$^{31,32}$ and deconvolution (matrix inversion) by the same operator. A R-P plot$^{31}$ is applied to the first few minutes of the renal and blood curves. The intercept of that plot ($F$) allows completion of the background subtraction process, and the slope ($K$) indicates what proportion of the blood curve is entering the kidney each second [Figure 1]. $H(0)$ is the initial retention function value, after elimination of blood background activity. In practice, it is best obtained either as the plateau value of the retention function [Figure 2], or as the slope of R-P plot (i.e., “$K$”) [Figure 1].$^{21}$ The R-P plot starts with an initial value and rises with a slope. The first proof of the R-P plot$^{38}$ actually demonstrated that the initial value was equal to the blood background subtraction factor “$F$” (the interception of the straight line with $y$-axis as shown in Figure 1), and that the slope was similar to the uptake constant “$H(0)$” (the plateau value as shown in Figure 2).

MATERIALS AND METHODS

Seventeen patients (32 kidneys), 10 male and 7 female (their ages range from 15 to 62 year), were referred for further evaluation by renal scanning. Eight kidneys were diagnosed to be obstructed by both radiological investigations (intravenous pyelo-graphy) and diuretic renography. As part of the preparation procedure, the patient should be well hydrated and the urinary bladder is emptied before the study. All patients were positioned supine with their backs to the scintillation gamma camera, so that the kidneys and the heart are both in the field of view. The camera used in this investigation is a Siemens type camera with 16” diameter NaI (Tl) crystal used in conjunction with a high-sensitivity parallel-hole collimator. Approximately 5-7 mCi of $^{99m}$Tc-DTPA in about 0.5 ml of saline is injected intravenously and dynamic sequential 20 s frames are acquired (64 × 64 matrix) and stored in a computer equipped with data analysis software. The study on each patient lasts for approximately 20 min. The time-activity curves of the parenchymal region of each kidney, as well as the heart were obtained for analysis. The data were then analyzed with deconvolution and the R-P plot. Both deconvolution and R-P plot approaches applied for the assessment of renal uptake, are based on the assumption that up to a given time after injection, corresponding to the minimum transit time, there is no output of activity from the renal region of interest (ROI).$^{35}$

RESULTS

Figures 2 and 3 represent the renograms and renal retention functions obtained by applying iterative deconvolution (matrix inversion) method, for left and right kidneys for one patient. Figure 1 demonstrates renal R-P plot. The $x$-axis is the integrated radioactivity in the blood for an ROI around the heart, divided by the radioactivity in the blood for that ROI during a certain time. The $y$-axis is the radioactivity in the kidney ROI during a certain time, divided by the radioactivity in the blood during the same time. Figure 4 demonstrates the relationship between the values of the renal uptake rate obtained by applying R-P method and the iterative deconvolution (matrix inversion) method. The regression equation of the R-P against iterative deconvolution (matrix inversion) was $Y = 1.18 X - 0.55$ ($r = 0.83$).
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and by the iterative deconvolution (matrix inversion) method

Figure 4: Scatter plots of renal uptake rate determined by Rutland-Patlak method and by the, iterative deconvolution (matrix inversion) method

Results (statistical analysis)
The scintigraphy uptake rate values determined by R-P method and by the iterative deconvolution (matrix inversion) method, were further analyzed to the method of Bland-Altman, which is a supplementary method to compare two different methods when the true value is unknown. The data was plotted as scatter plot of the mean values versus the difference of both calculations [Figure 5]. A plot of the mean of kidney uptake function calculations obtained by applying the two methods on 32 99mTc-DTPA renography (horizontal axis), versus the differences in the two calculations (vertical axis). The horizontal solid lines [Figure 5] indicate the mean difference between the two calculations. The horizontal dashed lines indicate the 95% limits of agreement (mean ± 1.96 standard deviation). Ninety seven percent of the values in the study (31 cases from 32 cases, 97% of the cases) were within limits of agreement. A strong positive association (n = 32; r = 0.83; R² = 0.68) was found between the values that obtained by applying the two methods [Figure 4].

The value of the uptake rate can be calculated from the slope of the straight line [Figure 1], for this patient the slopes are equal to 4%/min for the left kidney and is equal to 8%/min for the right kidney. Whereas the values of the uptake rate obtained by applying the deconvolution method are equal 3%/min and 5%/min for the left and right kidneys, respectively, which are equal the value of the plateau of the retention function [Figure 2]. From Figure 2, we noticed that the excretion of the radioactivity from the right kidney (normal) began earlier than that of the left kidney (obstructed). It took approximately 4 min to begin for the right kidney, whereas it took approximately 12 min for the left kidney.

DIscussioN

Deconvolution and the R-P plot have been widely used for analysis of renography, each enabling the derivation of renal uptake corrected for vascular background contribution. Rutland[1] have shown that the two methods for uptake measurement are theoretically equivalent, in this article the two methods have validated in practice in a series of 32 renograms that cover a wide variety of ages. Theoretically, the deconvolution method

is an ideal method for the estimation of renal transit.[16,39-41] In practice, however, there are many physiological and technical factors that hamper the proper application of deconvolution analysis to the renogram.[10,19] Indeed, the conditions that need to be met for deconvolution are not entirely fulfilled. The linearity of the system is not respected when the precordial curve is used as the input function, as it differs from the true plasma curve. The required stationary condition, on the other hand, is violated by changes in renal emptying due to back-pressure of the bladder. An abrupt change in urine flow due to the injection of a diuretic during the acquisition totally invalidates the deconvolution analysis.[28] The R-P plot has now been around for over 20 years, which poses the question of why it has taken so long for this relationship to be made evident? There are two likely reasons. Firstly, that the other forms of deconvolution were available, and so there was no great pressure to look for alternatives. The second is that in many of cases the R-P plot did not appear to have a level, but actually appeared to decline once tracer started to leave the organ. This will occur when the blood curve being used is not a true measure of arterial blood. That will occur in the later stages of externally measured blood curves when there is an excess of counts due to soft-tissue activity also being measured in the “blood” curve. It is possible that looking at the later stages of the R-P plot is a way of actually seeing how truly the externally measured blood curve matches the input function to the organ.[28] The reasoning behind this approach is that in producing the R-P plot, both the content function and the integral of the input function are divided by the input function (i.e., blood curve), and that this has the effect of producing data equivalent to that which would be produced if the input function did not vary (i.e., if there were a constant blood level of tracer).[29] The convolution technique (the iterative method) relies heavily on the accuracy of the first point analyzed (first point of the retention function as shown in Figure 1), as any errors are carried forward into the calculations of all the subsequent points, whereas R-P technique is based on an initial analysis of the data (four points which constitute the straight line as shown in Figure 3) by means of the R-P plot.[31,38] The conventional deconvolution methods
are iterative (or matrix inversion) deconvolution; or using either Laplace or Fourier transforms. Whichever method is used, all are very sensitive to small variations in the input data, making it difficult to prevent large errors developing. Furthermore, all these conventional methods first generate a retention function and then use that retention function to measure the uptake rate from the plateau height. [12] Whereas in R-P plot method, the uptake rate was calculated directly from the slope of the R-P plot straight line. In R-P plot the tracer concentration curves of tissue ROI and arterial plasma are transformed and combined into a single curve that approaches linearity when certain conditions are reached. The data could be plotted in a graph, and a curve can be fitted to the linear phase. The slope of the fitted line represents the net uptake rate of the tracer or volume of distribution. [13] The graphical analysis methods are independent of any particular model structure. [20]

CONCLUSION

There was a strong correlation between renal uptake values measured by R-P and iterative deconvolution methods. We believe that R-P analysis method is expected to be more reproducible than iterative deconvolution method, because the deconvolution technique (the iterative method) relies heavily on the accuracy of the first point analyzed, as any errors are carried forward into the calculations of all the subsequent points, whereas R-P technique is based on an initial analysis of the data by means of the R-P plot,[18,31] and we also believe that this technique can be considered as an alternative technique to find and calculate the renal uptake rate.

REFERENCES

1. Fleming JS, Kemp PM. A comparison of deconvolution and the Rutland-Patlak plot in renography analysis. J Nucl Med 1999;40:1503-7.
2. Britton KE. A technique for the deconvolution of the renogram. Physiol Med Biol 1974;19:546-9.
3. Diffey BL, Hall FM, Corfield JR. The 99mTc-DTPA dynamic renal scan with deconvolution analysis. J Nucl Med 1976;17:352-5.
4. Rutland MD. A comprehensive analysis of renal DTPA studies. I. Theory and normal values. Nucl Med Commun 1985;6:11-20.
5. Russell CD, Japanwalla M, Khan S, Scott JW, Dubovsky EV. Techniques for measuring renal transit time. Eur J Nucl Med 1995;22:1372-8.
6. Gates GE. Glomerular filtration rate: Estimation from fractional renal accumulation of 99mTc-DTPA (stannous). AJR Am J Roentgenol 1982;138:565-70.
7. Taylor A, Nally J, Aurell M, Blaufox D, Dondi M, Dubovsky E, et al. Consensus report on ACE-inhibitor induced nephropathy. J Nephrol 1996;9:187-82.
8. Kenny RW, Ackery DM, Fleming JS, Goddard BA. Grant RW. Deconvolution analysis of the scintillation camera renogram. Br J Radiol 1975;48:481-6.
9. Chaitawanant T, Padhy AK, Bomanji JB, Nimmon CC, Sommezzu K, Britton KE. Validation of renal output efficiency as an objective quantitative parameter in the evaluation of upper urinary tract obstruction. J Nucl Med 1993;34:845-8.
10. Whitfield MH, Britton KE, Hendry WF, Nimmon CC, Wickham JE. The distinction between obstructive uropathy and nephropathy by radioisotope transit times. Br J Urol 1978;40:433-6.
11. Whitfield HM, Britton KE, Hendry WF, Nimmon CC, Hendry WF, Wallace DM, Wickham JE. Renal transit time measurements in the diagnosis of ureteric obstruction. Br J Urol 1981;55:500-3.
12. Gonzalez A, Vigue F, Puchal R, Franco E, Bartrons R, Ambrosio S. Evaluation of renographic and metabolic parameters in human kidney transplantation. J Nucl Med 1997;41:4-2.
13. Nakagawa T, Maeda H, Terada N, et al. Clinical value of deconvolution analysis in radionuclide renal study. Radiat Med 1989;7:236-42.
14. Bajen MT, Martin-Comin J, Gonzalez A, et al. 99mTc-MAG3 renogram deconvolution analysis as a diagnostic aid in kidney graft monitoring. Transplant Proc 1995;27:2221.
15. Piepsz A, Ham HR, Erbsmann F, et al. A co-operative study on the clinical value of dynamic renal scanning with deconvolution analysis. Br J Radiol 1982;55:49-33.
16. Russell CD, Vester MV, Dubovsky EV. Measurement of renal parenchymal transit time of 99mTc-MAG3 using factor analysis. Nuclearmedizin 1990;29:170-6.
17. Kempi V, Sutton DG. Estimating the diagnostic yields resulting from renography and deconvolution parameters: A logistic regression analysis. J Nucl Med 1995;36:147-52.
18. Ham HR. Is renography suitable for deconvolution analysis? J Nucl Med 1996;37:403-4.
19. Kuyvenhoven JD, Ham H, Piepsz A. Is deconvolution applicable to renography? Nucl Med Commun 2001;22:1255-60.
20. Reive J, Crawley JC. Quantitative radioisotope renography: The derivation of physiological data by deconvolution analysis using a single-injection technique. Clin Sci Mol Med 1974;47:317-30.
21. Rutland M. Mean transit times without deconvolution reconsidered. Nucl Med Commun 2002;23:91-6.
22. Rutland M. Database deconvolution. Nucl Med Commun 2003;24:101-6.
23. Valentinuzzi ME, Montaldo Volaceee EM. Discrete deconvolution. Med Biol Eng 1975;13:123-5.
24. Diffey BL, Hall FM, Piepsz A, Erbsmann F. Renal deconvolution and the poor injection. Eur J Nucl Med 1978;13:45-6.
25. Britton KE, and Brown NJG. Clinical Renography. London: Lloyd-Luke; 1971.
26. Floyrae RI, Planeo T, Pursuile L. Le Nephrogramme et la Distribution des Temps de Transit. Annales de Physique Biologique et Medecine, 1972;6:1-6.
27. Appledorn, C.R., and B.E. Oppenheim. A Z-transform Approach to Renogram Deconvolution. In: Information Processing in Medical Imaging (Proceedings of the VII International Conference, Paris, 1979). Ed. by R. Di Paola and E. Kann, (INSERM, Paris), 1980;88:367-80.
28. Vester MV. Renal transit time. Glomerular filtration. In: Tauxe WN, Dubovsky EV, editors. Nuclear Medicine in Clinical Urology and Nephrology. Norwalk, Conn: Appleton-Century-Crofts; 1985. p. 90-5.
29. Vester MV. Evaluation of renal function: Computer programs and functional images. Nucl Physiol 1986:24-7.
30. Patlak CS, Blasberg RG, Fenstermacher JD. Graphical evaluation of blood-to-brain transport constants from multiple-time uptake data. J Cereb Blood Flow Metab 1989;7:71-7.
31. Peters AM. Graphical analysis of dynamic data: The Patlak-Rutland plot. Nucl Med Commun 1994;15:669-72.
32. O'Reilly PH, Shields RA, Testa HJ. Nuclear Medicine in Urology and Nephrology. London: Butterworth; 1979.
33. O'Reilly PH, Shields RA, Testa HJ. Nuclear Medicine in Urology and Nephrology. 2nd ed. London: Butterworth; 1986.
34. Al-Shakhrah IA, Yousef MK. Quantitative measurement of intrarenal mean transit time with deconvolution analysis using the matrix algorithm. Dirasat, for Natural and Engineering Sciences 1996;23:85-90.
35. Available from: http://www.turkupetcentre.net/modeling/methods/mgta.html#patak.
36. Available from: http://www.pnmol.com/technologies/doc/pk2326.htm.
37. Rutland MD. Single injection technique for subtraction of blood back ground in 131I-hippuran renograms. Br J Radiol 1979/52:134-7.
38. Grauembal SM, Nimmon CC, Nawaz MK, Britton KE. A non-invasive gamma-camera technique for the measurement of intrarenal flow distribution in man. Clin Sci 1981;61:385-9.
39. Wilkinson SP, Bernardi M, Pearce PC, et al. Validation of “transit renography” for the determination of the intrarenal distribution of plasma flow: Comparison with the microsphere method in the anesthetized rabbit and pig. Clin Sci Mol Med 1978;55:277-83.
40. Saito Z, Vorberg H, Sonnhaluz CA, Feinendegen LE. Model identification and estimation of organ-function parameters using radioactive tracers and the impulse-response function. Eur J Nucl Med 1985;11:265-74. How to cite this article: Al-Shakhrah IA. A comparison of deconvolution and the Rutland-Patlak plot in parenchymal renal uptake rate. Indian J Nucl Med 2012;27:176-80. Source of Support: Nil. Conflict of Interest: None declared.