Effect of Background Correction on Separate Technetium-99m-DTPA Renal Clearance

Amnon Piepsz, André Dobbeleir, and Hamphrey R. Ham

Departments of Radioisotopes, Hopital Saint-Pierre and AZ VUB, Free Universities, Brussels, Belgium

The estimation of the background constitutes the main difficulty in the accurate determination of the separate renal clearance, using the ^{99m}Tc-DTPA complex and the gamma camera. This is due to the low extraction rate of DTPA, giving an unfavorable signal-to-noise ratio, and to the fact that no background area can accurately represent both interstitial and vascular components of the renal curve. Several algorithms have been proposed in the literature for solving the problem of background but their effect on the calculated clearance value has not been sufficiently assessed. In this paper, it has been possible, using a theoretical approach, to predict the respective influence of the different algorithms on the renal clearance. These results were confirmed on the basis of clinical data obtained from 53 renal studies. it was shown that a double background correction, using successively the area ratio method followed by a linear fit method, is probably the most precise method and is less dependent on the choice of the background area.

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During these last years, several papers, dealing with the determination of the separate renal clearance of technetium-99m-diethyltriamnepentaacetic acid (^{99m}Tc-DTPA), have been published (*1–8*). Although the different algorithms which have been proposed for the calculation of the clearance are generally derived from the same equation, significant differences may be observed in the way they handle the problem of background. Several organs are superimposed to the renal area and contribute to the renal background:

1. At the upper pole of the kidneys, the liver, the spleen and the adrenals;
2. At the internal border, the large vessels and the duodenum;
3. At the external border, the gut;
4. Behind and in front of the kidney, several tissues including the skin, the muscles and the fat layer.

The renal background is composite and the problem of estimation of the true background is complicated because of the variable proportions of interstitial and vascular components in each organ, and from one individual to another. Some organs like the liver are well known to be much more vascularized than for instance the subrenal area, containing mainly interstitial tissue. These proportions depend also on the age of the patient: in young infants, the superposition of the liver and spleen is more important than in older people. It is, therefore, unlikely that one could define a region of interest (ROI) reflecting the exact contribution of the different organs. One can only hope, by choosing a ROI which is a compromise between the different structures, to approximate the true background. In the literature, several background areas have been proposed: liver (*3,9–10*); one pixel perirenal area (*1,7*), interrenal area (*11*), subrenal area (*4*), heart (*6,12–14*). Beside the choice of a given ROI as a representation of the intrarenal background, the respective amounts of intravascular and interstitial components of this background may be differently calculated using one or another method (*6,7,15*).

The aim of the present work was:

1. To compare theoretically the advantages and the biases of different correction methods.
2. To evaluate, on patient data, the effect on renal clearance of the different methods.

THEORY

Most of the algorithms allowing the calculation of the separate renal clearance by means of the gamma camera are modifications of the same equation:

$$R(t) = C \times \int P(t)dt.$$

Thus, the equation of the renal clearance can be expressed in two different ways:

$$C = R(t) \;/ \int P(t)dt \qquad (1)$$

or

$$C = dR(t)/dt \;/\; P(t), \qquad (2)$$

where:

C is the renal clearance.

R(t) is the "true" renal activity at time t, or the renal

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For reprints contact: A. Piepsz, Dept. of Radioisotopes, Hopital Saint-Pierre, 322, Rue Haute, B-1000 Brussels, Belgium.

activity completely corrected for background activity.

P(t) is the plasma activity at time t.

These equations are valid as long as no escape has occurred out of the renal compartment (t < minimal renal transit time).

When the tracer used for the clearance study is the ^{99m}Tc-DTPA complex, the low extraction rate of this tracer is responsible for the high background observed in the renal ROI and constitutes the main factor of error in the calculation of the true renal activity, R(t).

As the general profile of what is considered as the background curve is dependent on the choice of the background area, different clearance results can be expected for different background areas. Furthermore, the problem of background correction cannot be limited to the choice of the most adequate ROI. As a matter of fact, since the interstitial and vascular components are not the same in the background and in the renal areas, the problem still remains to determine what proportion (Q) of this background should be subtracted. Several approaches to this problem have been proposed in the literature and are discussed as follows.

Area Ratio Method

Ideally, if the chosen background area would represent exactly the true background in the renal area, the area ratio would adequately define the amount of background to be subtracted (*1*).

$$\begin{aligned} Rc(t) &= Rb(t) - Q \cdot Bg(t) \\ Q &= Sr/Sb, \end{aligned} \quad (3)$$

where:

Rc(t) is the background-corrected renal activity,
Rb(t) is the noncorrected renal activity,
Bg(t) is the activity in the background ROI,
Q is the coefficient defining the amount of background to be subtracted,
Sr and Sb are, respectively, the renal and background ROI surfaces.

Perirenal Background Area. We can assume that the interstitial activity in the perirenal area might represent the interstitial activity included in the renal area, and recent published data (*15*) tend to confirm this hypothesis. On the contrary, the angiographic data show clearly that the vascular supply is much higher in the kidney than around the kidney, so it is difficult to accept that the vascular component of the background is identical in the renal and the perirenal areas. It is therefore, probable that, using the slope method (Equation 2) for the calculation of the clearance, the area correction introduces a systematic bias by neglecting part of the vascular component. Since the vascular component is, like the plasma curve, a descending curve, the clearance value will be underestimated. On the contrary, when the integral method is used (Equation 1), an underestimation of the vascular component will give rise to an overestimation of the corrected renal counts and, by way of consequence, of the renal clearance.

Subrenal Background Area. If a subrenal area is chosen for the background correction instead of a perirenal area, one may expect a change in the renal clearance calculated by means of the slope method: the vascular component in this area is less important than in the renal and in the perirenal area and the area ratio method will, therefore, underestimate the clearance value.

Suprarenal Background Area. In the suprarenal area (liver and spleen), the vascular component is much more important than in the perirenal area and one might expect an overestimation of the renal clearance using the area ratio method and Equation 2.

The Adjustments Method at Time t = 80—140 sec

Rewriting the equation defining the renal clearance, C, results in:

$$Rc(t) = C \times \int P(t)dt;$$

We then call:

$$I(t) = \int P(t)dt$$

$$Rc(t) = C \times I(t) \quad (4)$$

If the clearance is constant during the small interval of time, when no escape has occurred out of the renal area, that is between 80–140 sec, then Rc(t) is proportional to I(t).

Taking into account Equations 3 and 4, one can write:

$$C \times I(t) + QBg(t) = Rb(t), \quad (5)$$

where I(t), Bg(t) and Rb(t) are known and directly measured and C and Q are unknown.

If I(t), Bg(t) and Rb(t) are replaced in Equation 5 by their numerical values, respectively for time 80, 100 and 120 sec, we obtain three equations with two unknowns, which can be resolved by the least squares method.

The theoretical advantage of this method is that the coefficient Q is calculated in order to be optimally adapted to time t80, t100 and t120, which are used for the calculation of the clearance. Unfortunately, another systematic bias can be expected using this method. Considering Equation 4, one can see that for t = 0, Rc(t) = 0, or in other words, the renal curve will, after this type of correction, necessarily pass by the origin. This means that, if a perirenal or a subrenal background area is used, the Q factor will be of greater magnitude than that with the area method and will introduce a greater scaling factor for both interstitial and vascular components—since the interstitial component is adequately estimated using the area method, it is, by way of consequence, overestimated using the adjustments method. The interstitial component curve being an ascending curve will introduce a systematic underestimation of the clearance using Equation 2. However, the suprarenal area does not contain enough interstitial activity and, for that reason, the use of this background area will give rise to an overestimation of the renal clearance.

Double Correction

This method is a combination of the area ratio method and the linear fit method. Different variants of this combination have been published (*6,7*). Rewriting the components of the renal background equation yields:

$$\mathrm{Rb(t)} = \mathrm{Rc(t)} + \mathrm{T(t)} + \mathrm{aP(t)}, \qquad (6)$$

where T(t) is the interstitial component and aP(t) the fraction of the blood pool included in the renal background.

The background activity, corrected for the area ratio, can be expressed as:

$$\text{background activity} = \mathrm{T'(t)} + \mathrm{a'P(t)}. \qquad (7)$$

In case of a perirenal background, the interstitial component included in the perirenal area is equivalent to the interstitial component in the renal area, thus: $T' = T$. Subtracting Equation 7 from Equation 6, dividing by P(t), and taking into account Equation 1 results is:

$$\frac{\mathrm{Rc(t)}}{\mathrm{P(t)}} = \frac{\mathrm{C}\cdot\int \mathrm{P(t)dt}}{\mathrm{P(t)}} + (\mathrm{a} - \mathrm{a'}). \qquad (8)$$

This is the equation of a straight line (Fig. 1) that can be obtained by applying a fit on several early points (t = 60, 80, 100, 120, 140 . . .). The slope of the line, C, is the renal clearance, corrected for interstitial as well as for vascular activity; the ordinate at origin, a−a′, is the fraction of vascular activity non corrected by the area ratio method.

This method combines the advantage of the area ratio method, which corrects adequately for the interstitial component, with that of the linear fit method, which eliminates the residual vascular activity not corrected by the area ratio method. It should theoretically give a better approximation of the true renal background, although it still relies on several assumptions like an arbitrary choice of the background ROI, or the hypothesis that perirenal and renal interstitial components are identical.

How will the double correction behave if a subrenal background area is chosen? Since the interstitial component is probably very similar in the subrenal and in the perirenal areas, the area ratio method similarly will correct this interstitial component. The part of the vascular component which has still to be corrected is different for both areas but will be adequately identified using the ordinate at origin of the linear fit. One can, therefore, predict that the value of the renal clearance will be very similar using any of these two areas. On the contrary, since the interstitial component is much less in the liver and spleen area than in the perirenal area, it is probable that this component will be undercorrected using the suprarenal background area and the double-correction method and that the slope of the linear fit will depend not only on the true renal clearance but also on the noncorrected part of the interstitial component. The result of this undercorrection will, therefore, be an overestimation of the clearance value.

MATERIALS AND METHODS

We have selected, on the basis of a wide range of clearance values, 53 good quality dynamic ^{99m}Tc-DTPA studies (106 kidneys), performed in clinical routine in adults and children. The gamma camera technique has been largely described in previous papers. The calculation of the clearance was based on the determination of the corrected renal curves and a

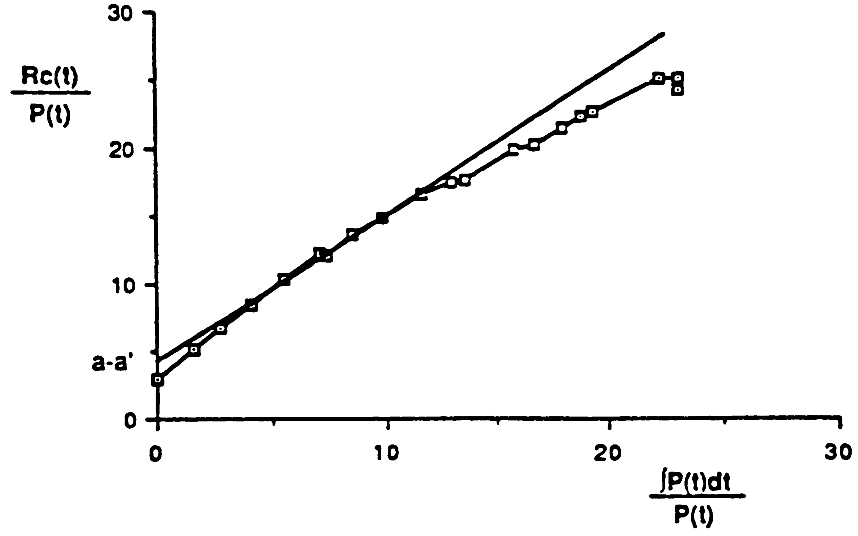

FIGURE 1
Graphic representation of Equation 8. The extrapolation of the linear fit does not pass by the origin. The ordinate at origin is a value a-a′, representing the part of the intrarenal vascular component not corrected by the area ratio method. The slope represents the clearance.

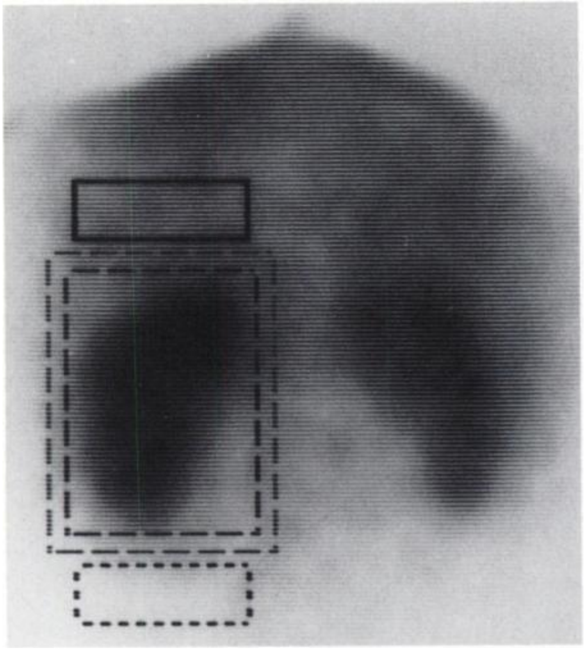

FIGURE 2
Regions of interest used in the present study: renal, perirenal, suprarenal, and subrenal areas.

plasma curve reconstructed from a calibrated heart curve (*1*).

Three different background areas were chosen (Fig. 2):

1. a suprarenal area (liver or spleen).
2. a one pixel perirenal area.
3. a subrenal area.

The amount Q of subtracted background was calculated using successively the three algorithms developed in the previous section.

RESULTS

Table 1 shows the results of the clearance calculated, for the 53 right kidneys, by means of the three different algorithms, using the perirenal area as the background area. In most of the cases, the double-correction method did provide the highest clearance results, compared to the area ratio method and to the adjustments method. The mean difference between the double-correction and the area ratio method was 5.7 ml/min (s.d. = 5.3 ml/min). No significant differences were observed between the area method and the adjustments method (Table 2).

Figure 3 shows the results of the clearance using successively the perirenal, the suprarenal, and the subrenal background regions. When the subrenal area was used, the clearance results using the area method were much lower than with the perirenal area and were often in the negative range. A similar but less pronounced underestimation of the clearance was observed when the adjustment method was used. However, the use of a subrenal background area instead of a perirenal area did not greatly influence the results with the double-correction method (Table 3). When the suprarenal area was used, the clearance results were much higher than with the perirenal area, whatever the chosen algorithm. The calculated data on the 53 left kidneys provided very similar conclusions.

DISCUSSION

The ^{99m}Tc-DTPA complex is widely used in clinical practice for the quantification of the separate renal function. Due to its low extraction rate, the main difficulty is related to the existence of a high background activity. For evident anatomic reasons, it is not possible

TABLE 1
^{99m}Tc-DTPA Right Kidney Clearance Calculated by Means of Three Different Algorithms Using Perirenal Background

No. of kidney	Surface ratio	Adjustment method	Double correction	No. of kidney	Surface ratio	Adjustment method	Double correction	No. of kidney	Surface ratio	Adjustment method	Double correction
1	37	43	50	19	6	9	10	37	20	22	24
2	74	70	75	20	87	89	102	38	31	31	35
3	120	135	131	21	79	77	84	39	160	240	206
4	32	32	34	22	54	55	54	40	15	14	13
5	32	24	29	23	0	3	3	41	67	78	74
6	20	11	14	24	43	44	46	42	97	93	103
7	32	33	39	25	61	63	68	43	57	59	59
8	95	94	88	26	31	35	43	44	48	44	51
9	57	56	56	27	38	39	36	45	36	33	32
10	7	17	12	28	42	38	35	46	2	3	3
11	77	77	84	29	23	25	25	47	41	42	43
12	72	86	85	30	24	8	21	48	6	8	8
13	27	23	27	31	8	9	10	49	7	6	5
14	23	24	31	32	19	22	25	50	5	4	2
15	93	92	111	33	4	6	8	51	40	36	42
16	26	22	20	34	50	54	54	52	−1	0	1
17	16	14	11	35	46	45	52	53	35	35	43
18	31	28	38	36	51	45	46				

TABLE 2
Comparison Between Area Ratio, Adjustment, and Double-Correction Methods Using Successively the Perirenal, Subrenal and Suprarenal Background Areas

	Perirenal area	Subrenal area	Suprarenal area
Surface Ratio	R NS	R*	R*
vs.			
Adjustments	L NS	L*	L*
Adjustments	R*	R*	R NS
vs.			
Double Correction	L*	L*	L NS
Surface Ratio	R*	R*	R*
vs.			
Double Correction	L*	L*	L*

Paired Student t-test on the mean values of the clearances, after performing analysis of variance; p values are corrected for multiple comparisons.
NS = $p > 0.05$.
$p < 0.05$.
*$p < 0.01$.
R = right kidney; L = left kidney.

TABLE 3
Comparison Between the Three Background Areas Using Successively the Area Ratio Adjustment and Double-Correction Methods

	Surface ratio	Adjustment	Double correction
Perirenal	R*	R*	R NS
vs.			
Subrenal	L*	L*	L NS
Perirenal	R*	R*	R*
vs.			
Suprarenal	L*	L*	L*
Subrenal	R*	R*	R*
vs.			
Suprarenal	L*	L*	L*

*$p < 0.01$; NS = $p > 0.05$; R = right kidney; L = left kidney.

to find a ROI that would accurately represent the true renal background and would correctly take into account both interstitial and vascular components of this background. Theoretically, one can predict that both the area method and the adjustments method will give rise to an underestimation of the renal clearance—the area method underestimates the vascular component, whereas the adjustment method overestimates the interstitial component. In a large series of patients, we have shown that the double-correction method gives systematically higher clearance results than the two other methods, although the mean difference represents only 10%. From this observation, we cannot conclude that the double correction constitutes the ideal method. Actually, this last method relies at least on two assumptions:

1. The interstitial component is the same in the renal area and in the background area.
2. The vascular component in the renal area behaves exactly like the plasma curve obtained from the calibration of the heart curve.

However, the results obtained by means of this method are probably closer to the true background estimation and are less dependent on the choice of a given background area in that moving the background area from the perirenal to the subrenal area only slightly modifies the results of the clearance, whereas the same shift will produce a considerable change in the results obtained by means of the other two algorithms. The vascular component of the liver and spleen area is much higher than in the renal area. This explains the important

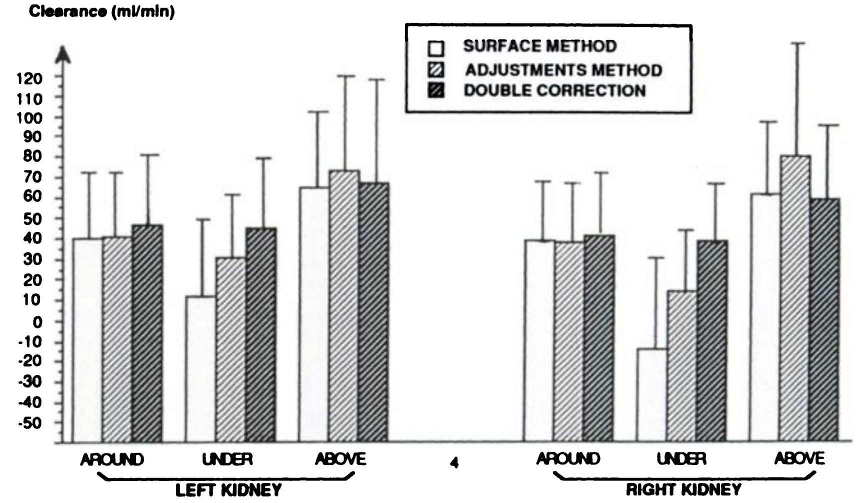

FIGURE 3
Mean clearance values calculated for 53 left and right kidneys using three different methods for the calculation of the background and three different background areas: around, under, and above the kidney. The mean and one s.d. are represented.

clearance overestimation which was observed using any of the three algorithms.

CONCLUSION

The determination of the renal clearance by means of the gamma camera and the ^{99m}Tc-DTPA complex necessitates a correction of the important nonrenal activity included in the renal area. The equations used in this paper for the calculation of the clearance imply an accurate estimation of this background activity.

It is relatively unimportant to use one or another type of background algorithm when the perirenal area is chosen as background area. The double correction algorithm is, however, the most precise method when the subrenal area is used. It probably provides the most accurate results, owing to the important systematic underestimation related to the use of the two other algorithms. The use of a suprarenal area will give rise to important errors on the clearance, whatever the method of background correction.

Finally, it should be noted that the methodology employed in this work, to determine the ideal background correction method, is entirely applicable to other renal tracers, such as ^{99m}Tc-MAG3, although the amplitude of the discrepancies will probably be less important for this tracer, owing to the better signal-to-noise ratio.

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