Quantification of Renal Uptake of Technetium-99m-DTPA Using Planar Scintigraphy: A Technique That Considers Organ Volume

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We developed a method to estimate the radioactivity of ^{99m}Tc-DTPA within the kidney by planar scintigraphy. Phantom experiments and renal studies were used to compare our method with that of the Gates' method. Our method corrects for scatter and attenuation using the volume depth-independent buildup factor technique, after which background correction is performed with consideration for target organ volume. When the renal phantom-to-background activity concentration ratio (S) was changed from 5 to 80 in a water-filled container and the renal phantom depth was varied from 1 to 11 cm for each value of S, the renal phantom count rate calculated by our method was accurate under all conditions investigated. In contrast, the Gates' method was significantly affected by phantom depth and S values. In 40 patients, renal uptake in the image obtained 2–3 min after injection of ^{99m}Tc-DTPA was estimated by our method and the Gates' method, and the correlation between uptake and creatinine clearance was determined. When a ring background region of interest (ROI) around the kidney was employed, a good correlation was obtained by our method ($r = 0.947$) in comparison with the Gates method ($r = 0.887$). With both methods, a semilunar background ROI produced poor results than the ring background ROI. In conclusion, renal radioactivity levels that correlate well with creatinine clearance can be obtained by our method, which allows estimation of individual glomerular filtration rates.

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Many investigators have attempted to quantitate renal function by using planar scintigraphic images. Schlegel et al. (*1*) measured effective renal plasma flow (ERPF) using ^{131}I-hippuran images with renal depth. Many authors have also tried to quantitate renal function with blood sampling. Tauxe et al. (*2*) measured ERPF and Constable et al. (*3*) measured glomerular filtration rate (GFR) with blood sampling. Though their methods could estimate renal function more precisely than those without blood sampling, blood sampling methods took much more time (*2,3*). Gates (*4,5*) estimated GFR using a linear relationship between renal uptake of ^{99m}Tc-diethylene triamine pentaacetic acid (DTPA) over 2–3 min and 24-hr creatinine clearance. Because the Gates' method simply estimates GFR using scintigraphic images without blood sampling, it has some problems achieving quantification of renal radioactivity (*6,7*) such as scatter and attenuation corrections, background subtraction and estimation of kidney depth. We have developed a method to estimate renal radioactivity using planar scintigraphic images (*8*). This method includes two corrections: (1) correction for scatter and attenuation using the volume depth-independent buildup factor (volume DIBF) technique and (2) background correction that is performed utilizing renal volume.

The purpose of this study was to evaluate our method in a kidney phantom experiment and a clinical study in comparison with the original Gates' method. Renal uptake estimated by our method and the Gates' method was correlated with creatinine clearance. In addition, the use of a ring background region of interest (ROI) around the kidney was compared with a semilunar background ROI below the kidney when calculating renal uptake.

THEORY

Scatter and Attenuation Correction

Photons emitted from a source in a medium undergo scattering and attenuation before reaching an external detector. To allow accurate correction for these changes, Siegel et al. (*9*) have proposed the DIBF technique. This technique employs a transmission factor defined as:

$$TF = 1 - \{1 - \exp(-\mu d)\}^{B(\infty)}, \qquad \text{Eq. 1}$$

where μ is a linear attenuation coefficient, d is the depth of a source and $B(\infty)$ is the buildup factor at infinite depth. However, the parameter TF in Equation 1 is only adequate for thin sources and cannot be used for thick sources.

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Therefore, we defined volume TF (TF_v) for thick sources as follows:

$$TF_v = \int_d^{d+t} TF\, dx$$

$$= 1 - 1/t \int_d^{d+t} [1 - \exp(-\mu x)]^{B(\infty)}\, dx, \quad \text{Eq. 2}$$

where t is the thickness of a volume source. The true count rate (C_t) is estimated as:

$$C_t = C_p/TF_v, \quad \text{Eq. 3}$$

where C_p is the measured count rate corrected for background activity.

Background Activity Correction

Conventionally, the following equation has been used to correct for background activity:

$$C_p = C - C_{bg}, \quad \text{Eq. 4}$$

where C_p is the corrected count rate, C is the count rate measured at the source area and C_{bg} is the background count rate normalized to the source area. However, since the parameter C_p in Equation 4 does not account for background activity in relation to the source volume, it underestimates the true count rate. As the source becomes thicker and/or the background activity increases, this underestimation becomes greater. Therefore, we corrected for such underestimation as follows (*8*):

$$C_p = C - C_{bg} + C_{bgc} \quad \text{Eq. 5}$$

$$C_{bgc} = C_{bg} \exp(\mu_0 d)[1 - \exp(-\mu_0 t)]/[1 - \exp(-\mu_0 T)], \quad \text{Eq. 6}$$

where d is the depth from the surface of the background to that of the source, t is the source thickness, T is the background thickness and μ_0 is the narrow linear attenuation coefficient.

MATERIALS AND METHODS

All studies were performed using a single gamma camera (ZLC-37-ECT, Siemens, Gammasonic, Inc., Des Plaines, IL) equipped with a low-energy, high-resolution, parallel-hole collimator. The field of view was 38 cm, and the camera was interfaced to a nuclear medicine computer system (Scintipac 2400, Shimadzu, Kyoto, Japan). Technetium-99m-pertechnetate was used for the phantom studies and ^{99m}Tc-DTPA for the clinical studies. Planar images were obtained using a 20% photopeak energy window centered at 140 keV. Image data were collected using a 64 × 64 matrix with a pixel size of 5.4 mm. A 25 × 20 × 25 cm tall lucite box was prepared as a container for the phantom study and a 180-ml renal phantom (KS type, Kyoto Kagaku, Kyoto, Japan) was placed into this container.

Forty hospitalized patients (20 men and 20 women, average age: 47 yr, range: 20–77 yr) with renal dysfunction underwent radionuclide renography. Twenty-four hour creatinine clearance values were also obtained in these patients within a week of the radionuclide study.

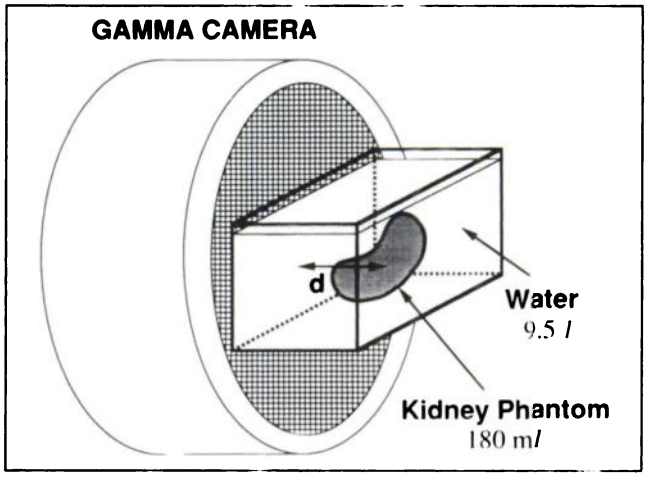

FIGURE 1. Experiments using a renal phantom. The gamma camera was placed in the lateral position.

Thin Sources

Three thin rectangular sources [20 cm^2 (4 × 5 cm), 40 cm^2 (5 × 8 cm) and 60 cm^2 (6 × 10 cm)] were prepared to determine the parameters μ and B(∞) in Equation 1. These sources contained 7.4 MBq (200 μCi), 14.8 MBq (400 μCi) and 22.2 MBq (600 μCi) of ^{99m}Tc, respectively. They were imaged in air and in water of various depths (1–11 cm) inside the container. Three rectangular ROIs corresponding to the cross-sectional areas of these thin sources (63, 129 and 193 pixels) were drawn on the source images semi-automatically.

A syringe containing 26.6 MBq (720 μCi) of ^{99m}Tc was counted in air using the gamma camera before injection into the renal phantom. To investigate the effect of background activity on the estimation of renal phantom activity, the background activity level was varied so that the phantom-to-background activity ratio (S) had five different values (5, 10, 20, 40 and 80). The renal phantom was imaged at various depths (3–11 cm) in the container for each value of S (Fig. 1). With these data, we calculated the count rate (C_e) in the phantom with the following two methods:

1. Attenuation correction with an attenuation coefficient of 0.15 cm^{-1} and conventional background subtraction (the Gates' method).
2. The volume DIBF technique and background correction with consideration for renal volume (the volume method).

We calculated the C_e-to-C_t ratio at each depth for each value of S, where C_t was the true phantom count rate obtained from the syringe count rate.

Clinical Study

Technetium-99m-DTPA (185 MBq, 5 mCi) was rapidly injected intravenously in the supine position. Posterior images were serially acquired with a 64 × 64 matrix and a frame rate of 30 sec per image over a 21-min period. The preinjection and postinjection syringe counts were measured with the gamma camera to obtain the net injected dose. No deadtime occurred in measuring these syringe count rates. The 2–3 min data were used as in the Gates' method (*4,5*). The kidneys were outlined to determine renal ROIs either manually or semi-automatically. In addition, both semilunar and ring-shaped ROIs were placed adjacent to the kidneys as

background ROIs (Fig. 2). Total renal uptake was calculated by the same two methods used in the phantom study and was correlated with creatinine clearance. The regression lines between the estimate of renal uptake and creatinine clearance were calculated for each method and were used to obtain GFR values. Significant differences between standard errors of the estimate (s.e.e.) were assessed using the F-test.

TF_v was calculated for all patients using the thickness, cross-sectional area and depth of each kidney. A summary of patient data is shown in Table 1. There were no statistically significant differences between right and left kidney data.

Data Analysis

According to Siegel et al. (*9*), the parameter B(∞) is constant for any source with an energy window, whereas the parameter μ varies as a function of the cross-sectional area of a source as follows:

$$\mu = \mu_0 \exp(-kA), \qquad \text{Eq. 7}$$

where A is the cross-sectional area and k is the constant. It was therefore necessary to determine constant values for k and B(∞) in our clinical study, which were calculated as follows. First, the datasets of (count rate in water)/(count rate in air) at various depths for three thin sources with a different area A (20, 40 and 60 cm^2) were fitted by Equation 1 using a nonlinear least squares technique and the values of μ and B(∞) for each area A were determined. Second, from three values of μ for three areas of A, k was determined using a linear least squares technique ($\log_e \mu = -kA + \log_e \mu_0$ and $\mu_0 = 0.15\ cm^{-1}$), and B(∞) was obtained as the mean of three values of the calculated B(∞). By using the mean value of B(∞) and the value of μ calculated with Equation 7 for an arbitrary renal area, TF_v was calculated for each kidney with a numerical integration technique.

RESULTS

The Parameters μ and B(∞)

The values of the parameters μ and B(∞) for three different source sizes are listed in Table 2. From these data, B(∞) and k were determined to be 1.263 ± 0.012 and $1.261 \times 10^{-3}\ cm^{-2}$, respectively. TF_v was then calculated for the kidney phantom and for patients' kidneys with these values.

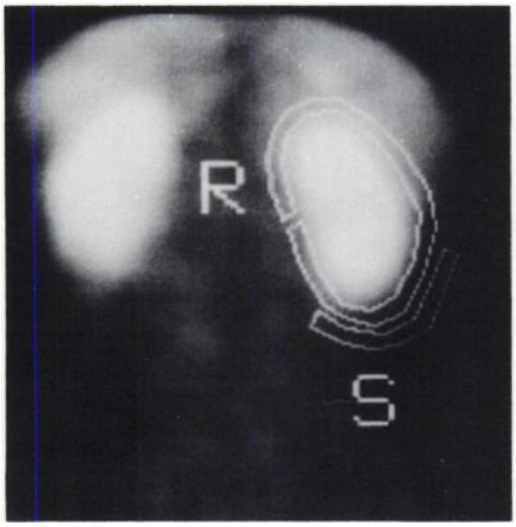

FIGURE 2. Sites of the ring background ROI and the semilunar background ROI.

TABLE 1
Summary of Measured Patient Data Using Posterior and Lateral Images and TF_v Values

	Measured size (mean ± s.d.)		
	Right kidney (n = 38)	Left kidney (n = 40)	Body (n = 40)
Depth (cm)	6.75 ± 1.08 (4.2; 9.0)*	6.90 ± 1.10 (4.1; 9.2)*	
Thickness (cm)	4.58 ± 0.85 (2.8; 7.1)*	4.58 ± 0.78 (3.0; 6.9)*	
Cross-sectional area (cm^2)	32.06 ± 6.94 (21.2; 50.4)*	34.88 ± 8.13 (21.2; 64.1)*	
Body thickness (cm)			19.61 ± 2.40 (13.2; 27.8)*
TF_v value	0.342 ± 0.050 (0.236; 0.452)*	0.333 ± 0.051 (0.230; 0.482)*	

*Minimum, maximum.

Renal Phantom Study

The ratio of C_e-to-C_t is plotted in Figure 3 versus depth and at different values of the S ratio. The Gates' method showed a tendency to overestimate the true count rate as the depth increased and the S value became higher. In contrast, the volume method accurately estimated true count rates for all depths and all S values.

Clinical Study

The correlation of total renal uptake rate with creatinine clearance was calculated for the volume method and the Gates' method (Table 3). The difference between the ring background ROI and the semilunar background ROI was also assessed. Use of the ring background ROI gave a better correlation than the semilunar background ROI, and the volume method produced better results than the Gates' method (Fig. 4). The error for the volume method using a ring ROI was significantly lower than that for the Gates' method using ring and semilunar ROIs ($p < 0.05$). There was no statistically significant difference between errors in the volume methods using ring and semilunar background ROIs.

DISCUSSION

Renal function has been evaluated using radionuclide and scintigraphic images by a number of workers. Tauxe et al. (*2*) used ^{131}I-hippuran to estimate ERPF with blood

TABLE 2
Values of μ and B(∞) for Three Thin Rectangular Sources

	Area (cm^2)		
	20 (5 × 4)	40 (8 × 5)	60 (10 × 6)
μ	0.145	0.142	0.139
B(∞)	1.272	1.267	1.250

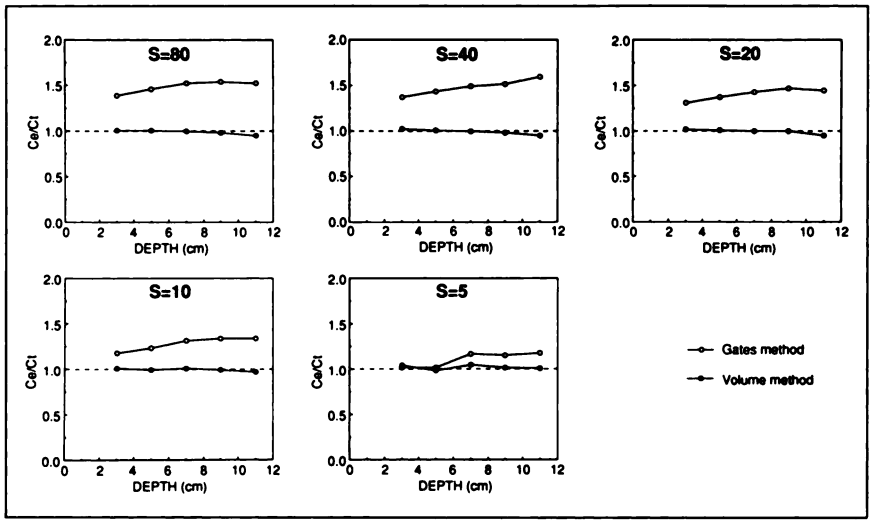

FIGURE 3. The ratio of estimated counts-to-true counts plotted against kidney depth for various renal phantom-to-background activity ratios (S). The broken lines show the true ratio.

sampling 44 min after injection, and Constable et al. (*3*) measured GFR using ^{99m}Tc-DTPA with blood sampling at 3 hr after injection. Although their method could estimate renal function precisely, blood sampling techniques took much time. In Japan, uptake methods are broadly accepted in clinical use.

Schlegel et al. (*1*) calculated ERPF using ^{131}I-hippuran without blood sampling while considering renal depth. Gates (*4*) developed a method to calculate GFR from the renal uptake rate of ^{99m}Tc-DTPA. He used a narrow attenuation coefficient of 0.153 cm^{-1} for attenuation correction and performed simple conventional background subtraction with a semilunar background ROI in the inferolateral region of each kidney (*4,5*). Although he reported a good correlation between renal uptake and creatinine clearance, Fawdry et al. (*6*) and Ginjaume et al. (*7*) pointed out that the Gates' method was subject to uncertainty regarding background subtraction and the estimation of kidney depth. They reported that a semilunar shaped background ROI did not appear as real background activity and that Tønnesen's formula did not correctly show individual kidney depth. Therefore, if renal radioactivity could be estimated more accurately by a sophisticated method, it then could be used to predict renal function more precisely. We have developed a method that estimates the radioactivity within an organ from planar scintigraphic images. In phantom studies, we confirmed that it could accurately correct for attenuation and scatter as well as for background activity (*8*). We have now shown the method's ability to estimate true renal uptake of ^{99m}Tc-DTPA.

When estimating radioactivity within a volume source with background activity, there are two major problems: (1) attenuation and scatter and (2) background activity.

To correct for attenuation and scatter, many investigators have used a broad source attenuation coefficient instead of a narrow one (*11–15*) and the method involving the buildup factor (*9*). Siegel et al. (*9*) proposed the DIBF technique to solve these problems. The DIBF technique makes it possible to accurately correct for attenuation and scatter from a thin source at various depths. They reported that TF may vary with source size, energy window and collimator type (*9*). That is, although the parameter $B(\infty)$ is constant for any source with an energy window, the parameter μ varies as a function of the cross-sectional area of the source (A) as shown in Equation 7. The results of our calculation of TF also showed the accuracy of the technique. However, since the DIBF technique using TF is only adequate for thin sources, improvements are needed to account for source volume. We therefore developed TF_v as defined in Equation 2 to allow for source volume. Kidney thickness and depth are needed to calculate TF_v, so we measured renal depth and renal thickness using lateral scintigraphy. Renal depth in the Gates' method was estimated with Tønnesen's formula using body weight and height, although Hambye et al. (*16*) have reported that individual measurement on lateral scintigraphy is a more accurate way of determining kidney depth.

Because background activity is always present in clinical scintigraphic studies, it is necessary to perform background correction to obtain a target organ's activity. In routine practice, background counts generated near the organ are subtracted from the organ's ROI. However, with this correction method, the background counts for the region the organ occupies within the background are sub-

TABLE 3
Correlation Between Renal Uptake Rate and Creatinine Clearance for Two Different Background ROIs Using the Gates' and Volume Methods

	r	
	Gates' method	Volume method
Ring ROI	0.887	0.947
	(12.86)*	(9.66)*
Semilunar ROI	0.877	0.913
	(13.39)*	(11.75)*

*GFR s.e.e. = ml/min.

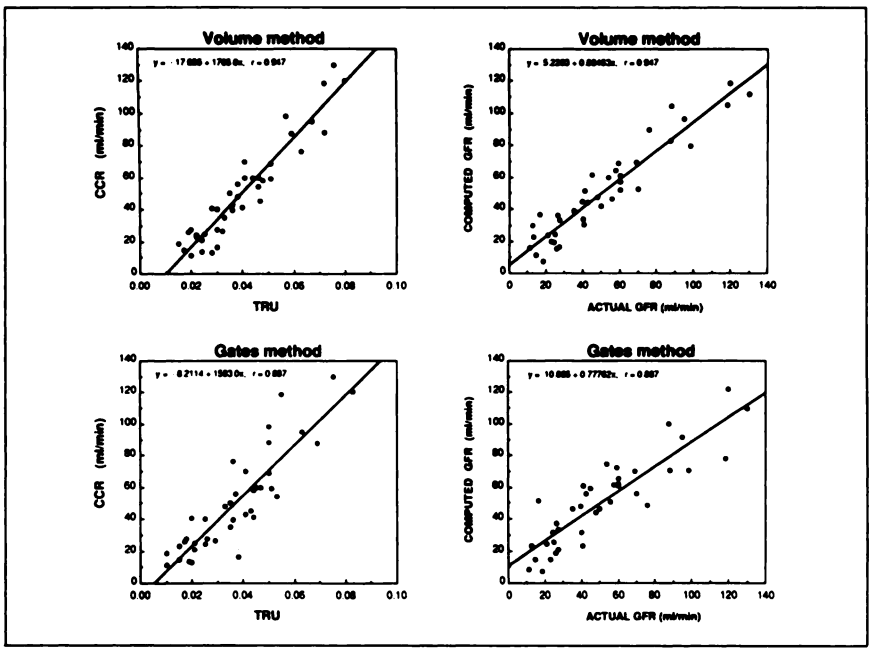

FIGURE 4. Correlations between creatinine clearance (CCR) and total renal uptake (TRU). Actual GFR and computed GFR for the two methods using the ring background ROI are shown.

tracted excessively. Accordingly, we corrected background activity by addition of oversubtracted counts. This method is similar to Schneider's method for estimating left ventricular volume (*17*). Our phantom study showed that the volume method could accurately estimate true count rate at various phantom-to-background activity concentration ratios. Ginjaume et al. (*7*) reported a poor correlation of the Gates' method with the true count rate (r = 0.37) and recommended the blood sampling method instead. Fawdry et al. (*6*) also preferred a blood sampling technique to the Gates' method. Although the blood sampling method was not used in this study, we obtained a strong correlation between renal uptake on planar images and creatinine clearance. This suggests that our volume method provides accurate information on renal function without the need for blood sampling.

Although Gates obtained a good result using a semilunar background ROI below each kidney, our data showed a poorer correlation than that obtained with a ring-shaped background ROI surrounding the kidney (Table 3). It is possible that the average counts in the ring-shaped background ROI more precisely represent background activity counts superimposed over the kidney. To perform our correction technique, renal size, depth and body thickness were determined for each patient by enhancing the contrast of the lateral images obtained after the dynamic study. Lee et al. (*18*) and Gruenewald et al. (*19*) have suggested direct measurement of kidney depth using lateral scintigraphy. Our volume method (*8*) was preliminarily applied to a clinical renal study using ^{99m}Tc-DTPA and useful information about GFR was obtained. The TF_v for each kidney can be easily calculated with a computer if the parameters k and B(∞) are predetermined from thin source measurements with a gamma camera and renal data acquisition conditions. The volume method appears to estimate renal uptake rates more accurately than the Gates' method, because the kidney has variable organ-to-background activity concentration ratios and depths. In addition, our method may be adapted to quantitate renal accumulation of other radiopharmaceuticals, such as ^{99m}Tc-MAG3 and ^{123}I-hippuran.

CONCLUSIONS

We evaluated a quantitative method for estimating renal uptake of ^{99m}Tc-DTPA in phantom experiments and clinical studies. This method differs from others in the following respects:

1. Renal depth and thickness and body thickness are measured on lateral view images.
2. Corrections for scatter and attenuation are done using the volume DIBF technique.
3. A more accurate method of background correction is used.

Our results showed that this method gives a better estimation of GFR than the Gates' method. It may become possible to accurately quantitate radioactivity within various organs with this method.

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