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Optimization of the uptake method for estimating renal clearance of 99mTc mercaptoacetyltriglycine

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Optimization of Uptake Method for Estimating Renal Clearance of ^{99m}Tc mercaptoacetyltriglycine

Running title:
Optimization of Uptake Method for MAG3 Clearance

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Abstract

Objective To improve the estimation of ^{99m}Tc mercaptoacetyltriglycine clearance in the renal uptake method by optimizing the conditions of renal depth, background, threshold for renal boundary determination, and time interval for integrating renal counts.

Methods Dynamic renal imaging was performed in 232 patients with dual energy window acquisition (main, 140 ± 14 keV; sub, 122.5 ± 3.5 keV). For drawing renal regions of interest (ROIs), cut-off methods with 50% and 70% of the highest renal pixel counts were used. For drawing the backgrounds, circumferential and lateral-inferior quadrant peri-renal ROIs were used. For setting the time interval, periods of 1--2, 1--2.5, 1.5--2.5, 1.5--3 and 2--3 min post-injection were used. For determining renal depth, three methods of a theoretical exponential function using scatter fraction, Tønnesen's formula, and linear combination of scatter fraction and Tønnesen's formula were used. The scatter fraction was calculated using the counts in renal ROIs in the two energy windows. Using every combination of these conditions, renal uptake was calculated. As a reference, one-sample clearance was calculated from a blood sample taken at 30 min post-injection following Bubeck's formula. According to the methods for estimating renal depth, three non-linear regression models were derived to convert renal uptake to clearance. Using one-sample clearance and integrated renal counts as dependent and independent variables, data were fitted to the models to determine the necessary constants. The correlations between the

model estimated clearances and one-sample clearance were investigated.

Results One-sample clearance ranged from 11 to 404 ml·min^{-1} per 1.73 m^2. More than half of the regression using renal depth determined by the scatter fraction alone failed to converge. Among the successfully converged regressions, all model estimated clearances showed significant correlations ($P < 0.01$) with one-sample clearance. The best correlation was observed in the model using renal depth determined by the combination of scatter fraction and Tønnesen's formulas, renal ROIs by 50% cut-off, lateral-inferior background and time interval of 2--3 min ($r = 0.898$, $P < 0.001$).

Conclusion The renal uptake method for estimating the clearance of mercaptoacetyltriglycine can be improved by the processing conditions proposed here.

Keywords: mercaptoacetyltriglycine (MAG_3), clearance, renal function, gamma camera

Introduction

^{99m}Tc mercaptoacetyltriglycine (MAG_3) dynamic renal imaging has been widely used in clinical work for its good imaging properties and low radiation exposure [1]. By processing the early images, the clearance of MAG_3 and the corresponding effective renal plasma flow can be estimated using the renal uptake method. However, it was thought to be less accurate than the blood sampling method [2] because the accuracy of the renal uptake method was closely associated with the processing conditions. To date, a number of processing conditions in the renal uptake method have been investigated and potential improvements have been suggested [3--16]. Some improvements in operator independent factors on the uptake method, such as the use of a more appropriate attenuation coefficient [8,12] and attenuation correction for the patient table [12] could increase the accuracy of the clearance estimation. However, the effects of other operator dependent conditions are still unclear. Therefore, we investigated four operator dependent conditions in the uptake method together, including the determination of renal depth, renal and background regions of interest (ROIs) and the time interval for integrating counts in the renal ROI, in order to improve the accuracy of the uptake method and to determine the optimal conditions for calculating clearance in a MAG_3 study.

Since the measurement of clearance by the plasma sampling method has been well developed and validated [2,17--19], as a reference, one-sample MAG_3 clearance obtained from Bubeck’s

formula was used.

Methods

Subjects

Two hundred and thirty-two patients (157 males, 75 females; mean age, 64 ± 17 years; age range, 9--91 years) with renal dysfunction in various degrees were studied by using ^{99m}Tc-MAG$_3$ dynamic renal imaging. There were three patients with a single kidney who had had renal excision. In another three patients, no accumulation of radioactivity due to severe renal dysfunction was found in two left and one right kidneys during the whole period of data collection. Therefore, these three patients were also regarded as having a single kidney. The study was approved by the hospital ethics committee and all patients gave their informed consent.

Radiopharmaceutical

^{99m}Tc-MAG$_3$ was prepared using a labeling kit (TechneMAG3®, Daiichi Radioisotope Laboratory, Tokyo, Japan) and ^{99m}Tc-pertechnetate freshly eluted from a ^{99m}Tc generator system (Ultra-TechneKow®, Daiichi Radioisotope Laboratory, Tokyo, Japan).

Imaging and Data Processing Protocol

A single headed digital gamma camera system equipped with a low energy general purpose collimator (RC-135E, Hitachimedico, Tokyo, Japan) was used for ^{99m}Tc-MAG$_3$ dynamic renal imaging. The in-plane spatial resolution of this system was 9.6 mm full width at half maximum in

the air. Dynamic acquisition with dual energy windows (main, 140 ± 14 keV; sub, 122.5 ± 3.5 keV) (Fig. 1) was begun immediately after the bolus intravenous injection of ^{99m}Tc-MAG$_3$ of 74--185 MBq according to the body surface area of the patients. Digital planar images were recorded at a frame rate of 60 frames/min for the first 3 min then at 6 frames/min for the following 27 min into a 64 × 64 matrix in the posterior position. The radioactivity of the pre-injection and post-injection syringes was measured with both a dose calibrator (IGC-7, Aloka Co. Ltd., Tokyo, Japan) and the gamma camera. By subtracting the radioactivity at post-injection from that at pre-injection, the injected dose was recorded in μCi for cases measured with a dose calibrator (D_{cal}) and in counts for cases measured with gamma camera (D_g).

Renal ROIs were drawn automatically on the left and right kidneys by 50% and 70% cut-off of the highest pixel counts on the merged reference images in the main energy window. For normally functioning and mildly dysfunctioning kidneys, the images from 60 to 120 s were merged, while for the severely dysfunctioning kidneys, the images from another 60 s time interval were added because of poor visualization of the kidneys. In a few cases, the renal ROI drawn automatically was not ideal because of the influence of high liver activity in early images and the renal pelvis in late images. Therefore, manual correction of the renal ROI was necessary in these cases. For background correction, the lateral-inferior quadrant and circumferential peri-renal background ROIs with about 2 pixel thickness were drawn manually, displaced about 3 pixels from the outer

margin of the renal ROIs determined by the cut-off level of 50% of the highest renal pixel count (Fig. 2). Time--activity curves and the sizes (pixel number) of these ROIs were recorded. From the image of sub-energy window, time--activity curves were also obtained based on the ROIs used for the images of main energy window. The background was normalized by multiplying the mean counts in the background ROI with the number of the pixels in the corresponding renal ROI. Then, normalized counts of background ROI were subtracted from the counts in the renal ROI to obtain background subtracted renal counts.

By analogy with the triple-energy window method [20], scatter correction was done for the background subtracted renal counts, c, in the main energy window. In the triple-energy window method, because the scatter from the high energy sub-window contributes only little to the counts in the main energy window, and most scatter comes from the low energy sub-window when using ^{99m}Tc, we used the counts in the low energy sub-window alone for the scatter correction. As shown in Fig. 1, background subtracted and scatter corrected renal counts, c_1, in the main energy window could be estimated from c and the background subtracted renal counts, c_2, in the scatter window as follows:

$$\begin{aligned} c_1 &= c - (c_2/w_s) \times w_m/2 \\ &= c - (c_2/7) \times 28/2, \end{aligned} \tag{1}$$

where w_s and w_m are the widths (in keV) of the scatter and the main energy window, respectively.

Then, using the linear attenuation coefficient of ^{99m}Tc in muscle (0.153 cm^{-1}) for attenuation correction, renal uptake, *U*, was calculated as below.

$$U = \{[(c_{1,L}/\exp(-0.153d_L)] + c_{1,R}/\exp(-0.153d_R)]\}/D_g, \quad (2)$$

where $c_{1,L}$ and $c_{1,R}$ are background subtracted, scatter corrected renal counts of the left and right renal ROIs in a certain integrating time interval; and d_L and d_R are the depths of the left and right kidneys, respectively.

For calculating the renal uptake, four conditions were investigated.

- *Renal ROI*: drawn by 50% and 70% cut-off of the highest renal counts (Fig. 2);
- *Background ROI*: lateral-inferior and circumferential peri-renal background (Fig. 2);
- *Time intervals for integrating renal counts*: 60--120, 60--150, 90--150, 90--180 and 120--180 s post-injection;
- *Renal depth*: three methods of estimating renal depth were adopted, as follows.

1. *The scatter fraction correction method*

The scatter fraction, *s*, was calculated from the counts of scatter divided by total counts in the main window as shown in Fig. 1:

$$s = c_s/c_{total}, \quad (3)$$

where c_s is the scatter counts in the main window and c_{total} is the total counts in the main window.

Our preliminary Mix-DP phantom study has proved that scatter fraction was exponentially increased as the depth of radioactive source was increased (Fig. 3) [21]. From this result, we ensured that renal depth could be expressed by the scatter fraction using the following equations.

$$d_{s,R} = \exp[(s_R - a_0)a_1], \quad (4)$$

$$d_{s,L} = \exp[(s_L - a_0)a_1], \quad (5)$$

where d_s refers to the renal depth determined by the scatter fraction method; R and L refer to right and left, respectively; a_0 and a_1 are unknown constants; and s_R and s_L are the scatter fractions of right and left kidneys, respectively.

2. *Use of Tønnesen's formula*

In this method the following equations apply:

$$d_{T,R} = 13.3W/H + 0.7, \quad (6)$$

$$d_{T,L} = 13.2W/H + 0.7, \quad (7)$$

where d_T refers to the renal depth determined by using Tønnesen's formula; and H and W are the height (in cm) and weight (in kg) of each patient.

3. *The linear combination method*

Here, the linear combination of scatter fraction and Tønnesen's formula are used to estimate

renal depth. In this method the following equations apply:

$$d_{comb,R} = b_0 (13.3W/H + 0.7) + b_1 s_R, \quad (8)$$

$$d_{comb,L} = b_0 (13.2W/H + 0.7) + b_1 s_L, \quad (9)$$

where d_{comb} refers to the renal depth determined by using the combination method; b_0 and b_1 are constants whose values are not known.

According to these three methods for determination of renal depth, renal uptake was corrected for the depth related photon attenuation. Therefore, the U in Equation 2, corrected by the scatter fraction, U_s, Tønnesen's formula, U_T, and linear combination of scatter fraction and Tønnesen's formula, U_{comb}, could be expressed as the following equations, respectively.

$$U_s = \{[c_{1,L}/\exp(-0.153 d_{s,L})] + [c_{1,R}/\exp(-0.153 d_{s,R})]\}/D_g, \quad (10)$$

$$U_T = \{[c_{1,L}/\exp(-0.153 d_{T,L})] + [c_{1,R}/\exp(-0.153 d_{T,R})]\}/D_g, \quad (11)$$

$$U_{comb} = \{[c_{1,L}/\exp(-0.153 d_{comb,L})] + [c_{1,R}/\exp(-0.153 d_{comb,R})]\}/D_g. \quad (12)$$

To optimize the four factors in the calculation of renal uptake, renal ROI, integration time for renal counts, background ROI and renal depth, every possible combination of proposed conditions for each factor was evaluated in terms of the correlation between renal uptake and reference clearance.

Referential one-sample clearance calculating using Bubeck's method

To change the value of the dose of ^{99m}Tc-MAG$_3$, which was measured as μCi with a calibrator (D_{cal}) to counts, a diluted aliquot of the ^{99m}Tc-MAG$_3$ preparation used for the study was measured with a well-type gamma counter (ARC-380, Aloka Co. Ltd., Tokyo, Japan) to determine the calibration factor, f, for converting μCi to counts.

At 30 min after the ^{99m}Tc-MAG$_3$ injection, a 2 ml blood sample was obtained from an antecubital vein contralateral to the side of radiotracer injection. After centrifugation at 1800 × $\boldsymbol{g}$ for 10 min, 500 μl plasma was drawn and counted with the same well-type gamma counter as used in the calibration for D_{cal} and then decay corrected plasma concentration of ^{99m}Tc-MAG$_3$ (c_p, counts/l) was obtained. Using counts calibrated D_{cal} and c_p, distribution volume, v (in litres), of MAG$_3$ at 30 min could be calculated as follows:

$$v = D_{cal} f / c_p. \tag{13}$$

Body surface area, A (in m^2), was calculated from the patient's weight (in kg) and height (in cm) using the empirical formula [22]

$$A = W^{0.425} \quad H^{0.725} \quad 0.007184. \tag{14}$$

Then, Bubeck's formula was applied to calculate one-sample MAG$_3$ clearance, C, at 30 min by using values for the distribution volume and body surface area:

$$C = -371.7 + 182.5 \ln(1.73\, v / A),$$

Where *ln* means $\log_e$

Statistical analysis

Using the value of one-sample clearance as a reference, three regression models according to the methods given for the calculation of renal uptake were formulated to convert renal uptake calculated by using the scatter fraction method (U_s), the Tønnesen formula (U_T), and the linear combination method (U_{comb}) to one-sample clearance as presented below.

Model 1, using the scatter fraction method,

$$C = E + FU_s; \tag{16}$$

model 2, using the Tønnensen formula,

$$C = E + FU_T; \tag{17}$$

model 3, using the linear combination method,

$$C = E + FU_{comb}, \tag{18}$$

where E and F are constants whose values are not known.

Using dedicated statistical software package (JMP 2.0, SAS Institute Inc., Cary, NC, USA), the prediction formulas with unknown parameters under all combinations of processing conditions according to the three methods of renal depth determination were fitted to the one-sample clearance by non-linear regression. The fitting was performed with a maximum limit of 60 iterations under the confidence level of $P < 0.05$ after the initial value of each parameter was set. Then estimated values of the parameters of E, F, a_0, a_1, b_0 and b_1 were determined when the

convergence of the fitting was successfully reached.

The correlation between the referential one-sample clearance, and the clearance calculated by the models was investigated. Fisher's *z* test was applied to test the difference between each two correlation coefficients.

RESULTS

The reference clearance ranged from 11 to 404 ml·min^{-1} per 1.73 m^2. In the fitting of model 1, fewer than half the fittings were successful. The highest correlation coefficient was 0.868. Correlation coefficients were not calculated in the regressions that failed to converge.

In the fitting of model 2, correlation coefficients ranged from 0.852 to 0.873. Correlation coefficients were improved by using late time intervals, peri-renal background and renal ROIs with 50% cut-off (Fig. 4).

In the fitting of model 3, correlation coefficients ranged from 0.879 to 0.898. Correlation coefficients were improved by using late time intervals, lateral-inferior background and renal ROIs with 50% cut-off (Fig. 5).

Among all the conditions investigated in the study, the best correlation coefficient was found in model 3, with an integration time of 120--180 s, 50% cut-off renal ROI and lateral-inferior background ROI (r = 0.898, P < 0.01, Fig. 6). By comparison with the best correlation coefficient, a few correlation coefficients in models 1 and 2 showed significant differences.

DISSCUSSION

Although estimation of renal function by a gamma camera technique was thought to be less accurate than the blood sampling method [2,23], this method could provide an important aid in the interpretation of dynamic renal imaging [12], enabling simple and rapid quantitative assessment of split renal function. Therefore, improving the accuracy of the uptake method is valuable and many investigators have concentrated their attention on this issue.

Referential one-sample MAG_3 clearance was calculated following Bubeck's formula because this method is simple and is thought to be sufficiently accurate for measuring renal function [2]. By this method, accuracy in the evaluation of renal function could be improved not only in adults but also in children [2]. In practice, the accuracy of a one-sample method depends on the time of sampling, and the optimum sampling time varies with renal function [24--28]. However, for the convenience of both patients and staff, the sample should be obtained as early as possible [29]. Bubeck *et al*. reported that the optimum time for blood sampling lies between 25 and 40 min in children and between 20 and 50 min post-injection in adults [2]. By referring to their results, we used the time of 30 min post-injection for blood sampling in both adults and children and believed this sampling time could be adequate for quantitative differentiation between normal and abnormal renal function.

Defining the renal ROI is necessary in the uptake method [6]. Usually, ROIs have been drawn

manually. However, inter-operator variability appeared to be inevitable with manual ROIs [30--34]. To reduce the operator's intervention, Inoue *et al*. reported a semi-automated method for drawing renal ROIs [6]. However, regardless of the method used for drawing renal ROIs, no suitable threshold has been well accepted for clinical use. To show the effect of threshold for the determination of renal ROI on the calculation of renal uptake, we used two simple thresholds for drawing renal ROIs. According to our results, using a renal ROI determined by the 50% cut-off provided a better evaluation of MAG_3 clearance than that obtained by using a 70% cut-off. The excessive loss of renal counts in the determination of renal ROI when using the 70% cut-off as a threshold might account for this finding. In patients with renal dysfunction, drawing renal ROIs by using a simple threshold appeared to be inappropriate because the kidney-to-background contrast at the early phase was low and usually associated with high liver uptake. Under this situation, a simple threshold tended to overestimate renal area, especially when using 50% cut-off as a threshold. In order to obtain good delineation of kidneys in these patients, we shifted the time interval properly to a later phase until the kidneys were well visualized and found the determination of renal ROI could be improved. However, renal ROIs drawn in either the early phase or late phase in some patients were not ideal because of the influence of high activity in the liver or renal pelvis, thus manual modification was inevitable. Our study confirmed the published findings that a simple threshold method was not ideal [6], although our results suggested that

using a lower threshold might be preferable for improving the calculation of renal uptake. A more accurate method remains to be found to determine the renal ROI without the influence of other organs and significant loss of renal counts.

Background correction has been commonly needed in the uptake method to assess true renal accumulation and assumes an increasing importance as renal function deteriorates [9]. Several studies found peri-renal ROI could better represent the actual background in the renal ROI [9--11]. Inoue *et al*. reported the types of background ROIs had little effect on the accuracy of calculated clearance [7]. Our results showed that all regression fittings using lateral-inferior background showed better correlations than those using peri-renal background when using renal depth estimated from the combination of scatter fraction and Tønnesen's formula (Fig. 5). On the contrary, all regression fittings using a peri-renal background showed better correlation when using renal depth estimated from Tønnesen's formula (Fig. 4). The different effects of background with different estimations of renal depth found in this study suggested there was close interaction between the determination of background and renal depth.

A previous study suggested that there would be no special problem if an one-minute interval from 1 to 3 minute was selected for integrating renal counts [4]. While Inoue *et al*. reported that the correlation was better when a later period was used for the calculation of renal uptake calculation, their results showed the accuracy was only mildly dependent on the periods, and the percent renal

uptake at different periods provided almost the same MAG_3 clearance [7]. In accordance with their findings, our results showed that using a later time interval could improve the correlation. Additionally, we found that the length of the time interval for integrating renal counts seemed to have no obvious effect on the calculation of renal uptake, while the starting point of time interval appeared to be important. Our results suggested that a later time interval before 3 min post-injection could provide a better estimation.

Soft-tissue attenuation correction has been required in evaluating absolute renal function [13]. An accurate estimate of renal depth is essential for soft-tissue attenuation [14]. Tønnesen's formula has been popularly used to calculate renal depth [35--38]. However, this formula has been found to underestimate renal depth [13,16]. Our previous study using a phantom has found that the depth of the radioactive source in scatter media could be expressed as an exponential function of scatter fraction [21]. Thus, based on this result, we used the scatter fraction for estimating renal depth and expected that this method could accurately reflect the individual differences of physical configuration and provide a satisfactory estimation. For comparison, Tønnesen's formula was also adopted. Unexpectedly, our results showed that among the three methods for the determination of renal depth, more than half of model fittings using scatter fraction alone failed to obtain convergence. The model fitting using the renal depth determined by the linear combination of scatter fraction and Tønnesen's formula showed obviously better correlations than the other two

model fittings, although most of the correlation coefficients showed no significant difference compared to the best one. This result implied that using scatter fraction for estimating renal depth could improve the evaluation of clearance. However, the weight and height of the patient should also be taken into consideration. The linear attenuation coefficient for ^{99m}Tc in muscle (0.153 cm^{-1}) was used for attenuation correction in the study. Although this value should be lower than 0.153 cm^{-1} due to the scatter [8,12,39--43], we adopted it as we considered that the fixed attenuation coefficient would have only a minimal influence when the other conditions were investigated in this study.

Li *et al*. found that the accuracy of clearance measurement deteriorated in the patients with glomerular filtration rate of <30 $ml \cdot min^{-1}$ [44]. Although they used ^{99m}Tc diethylenetriaminepentaacetic acid to estimate glomerular filtration rate and did not refer to Bubeck's method, their results suggested the blood sampling method might have its drawbacks when renal function was severely impaired. Since the one-sample clearance ranged widely, being from 11 to 404 $ml \cdot min^{-1}$ per 1.73m^2 in this study, and no patient was excluded, errors might have occurred in the estimation in the patients with severe renal dysfunction.

In the renal uptake method, calculation of early uptake post-injection is essential when determining MAG_3 clearance [4,12,45,46]. In this study, four operator dependent conditions, including renal depth, renal ROI, background, and time interval for integrating counts in renal

ROI for calculating renal uptake were investigated and the combination of these conditions was optimized. The determination of renal depth by considering scatter fraction was introduced and appeared to be superior to that obtained by using the classical Tønnesen's formula. In spite of the shortcomings in some parts of this study, the results demonstrated that the uptake method could be improved by selecting optimized processing conditions. Since the accuracy of the uptake method is not determined by the processing conditions only, future investigations concerning other factors would be useful.

CONCLUSION

This study found that the measurement of MAG_3 clearance by the uptake method could be improved. Although the exact conditions for the renal uptake method are hard to determine, our study suggests that using a lower threshold for the determination of the renal ROI, a lateral-inferior background, a value for renal depth determined from scatter fraction, the patient's height and weight, and the late time interval in the first 3 min post-injection are preferable for clinical use.

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Legend of Figures

Fig. 1 Dual energy window setting. The main window (M) was set from 126 to 154 keV and the sub-window (S) was set from 119 to 126 keV. Sc in the figure represents scatter in the main window. The scatter fraction was calculated from the total counts and the scatter in the main window, as given in Equation 3 (see text).

Fig. 2 Example of drawing regions of interest (ROIs) on a scan from a patient with an one-sample clearance of 272 $ml \cdot min^{-1}$ per 1.73 m^2. Seventy percent (arrows at position 1) and 50% (arrows at position 2) cut-off renal ROIs were automatically drawn in the left kidney. In the dysfunctional right kidney, renal ROIs were modified manually. The lateral-inferior quadrant (arrows at position 3) and peri-renal circumferential (arrows at position 4) background were drawn manually.

Fig. 3 Relation between scatter fraction and depth in the Mix-DP phantom study using ^{99m}Tc. The scatter fraction exponentially increased as the depth of the radioactive source increased.

Fig. 4 Correlation coefficients between one-sample clearance and calculated clearance in the model fitting with renal depth estimated by Tønnesen's formula. (A) Renal ROI with 50% cut-off; (B) renal ROI with 70% cut-off. Time = time interval for integrating renal counts. Pale bars: peri-renal background; dark bars: lateral-inferior background. $*P < 0.05$ compared with the highest correlation coefficient.

Fig. 5 Correlation coefficients between one-sample clearance and calculated clearance in the

model fitting with renal depth estimated by linear combination of the scatter fraction and Tønnesen's formula. (A) Renal ROI with 50% cut-off; (B) renal ROI with 70% cut-off. Shadings as in Fig. 4.

Fig. 6 Correlation between one-sample clearance and calculated clearance under the conditions of the renal depth determined by the combination of the scatter fraction and Tønnesen's formula, renal ROI by 50% cut-off, peri-renal background and an integrating time of 2--3 min. *n* = number of patients.

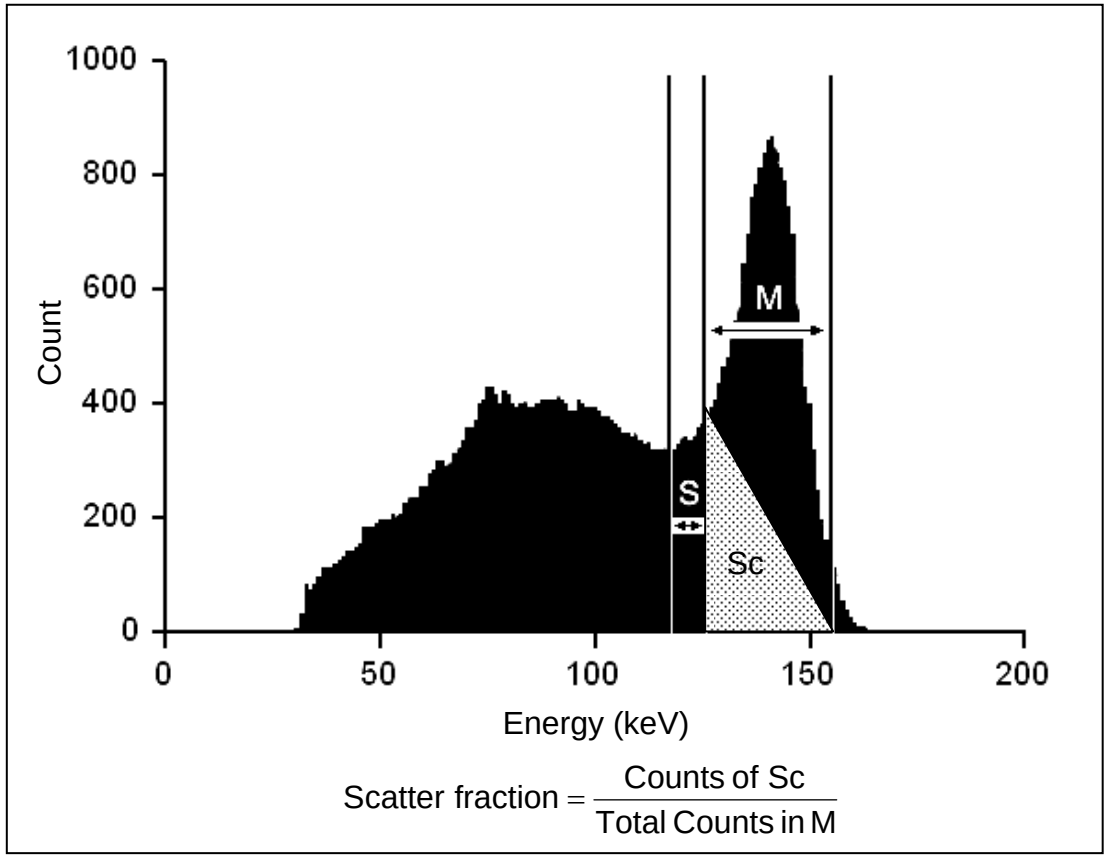
1000
800
600
400
200
0
Count
0
50
100
150
200
Energy (keV)
M
S
Sc
Scatter fraction = Counts of Sc / Total Counts in M

Figure 1

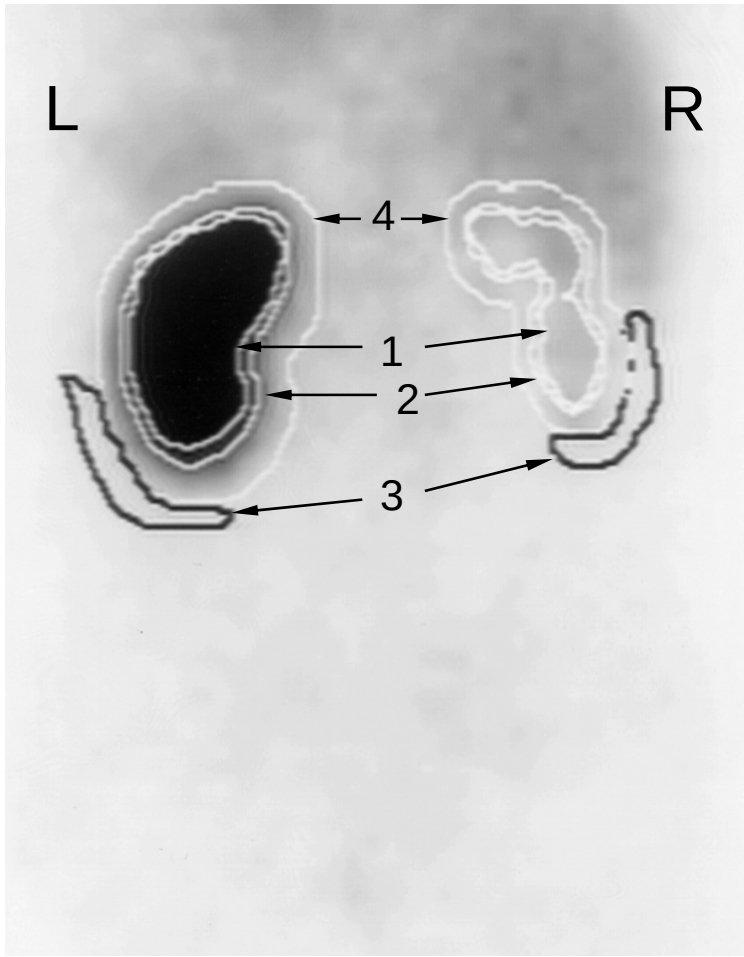

Figure 2

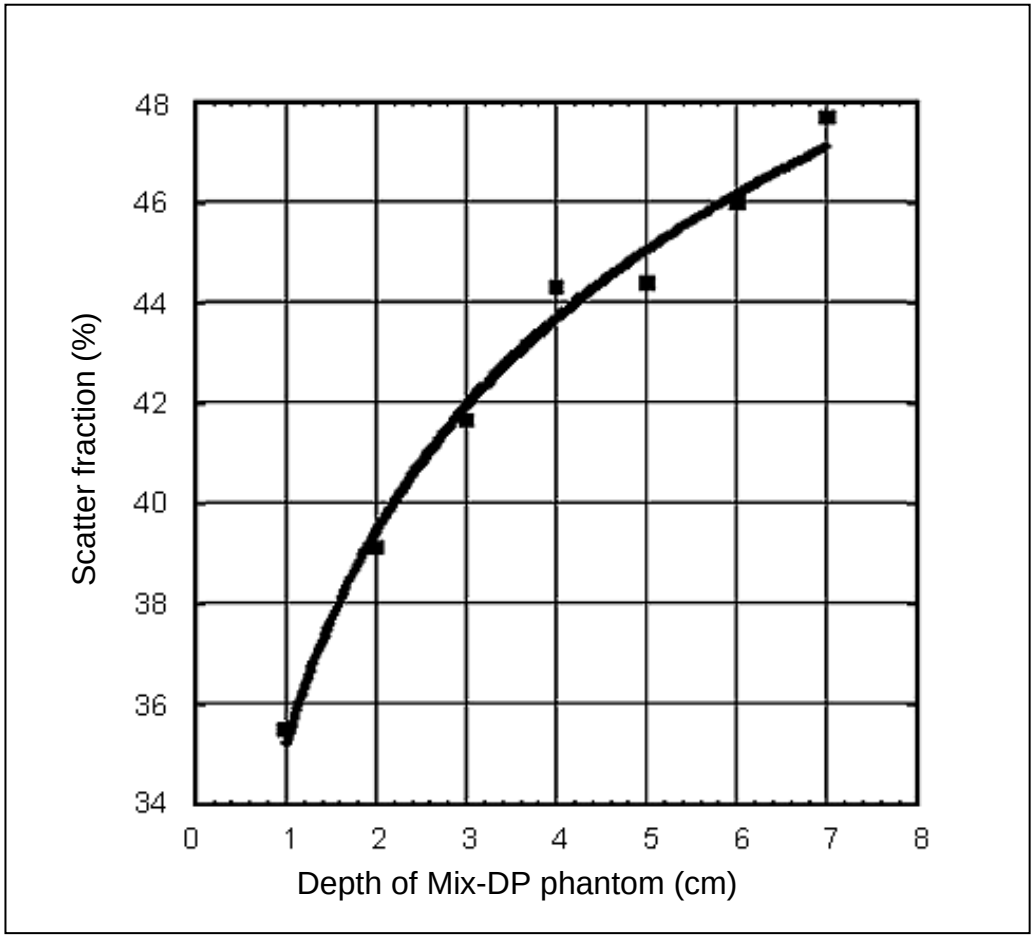
48
46
44
42
40
38
36
34
Scatter fraction (%)
0
1
2
3
4
5
6
7
8
Depth of Mix-DP phantom (cm)

Figure 3

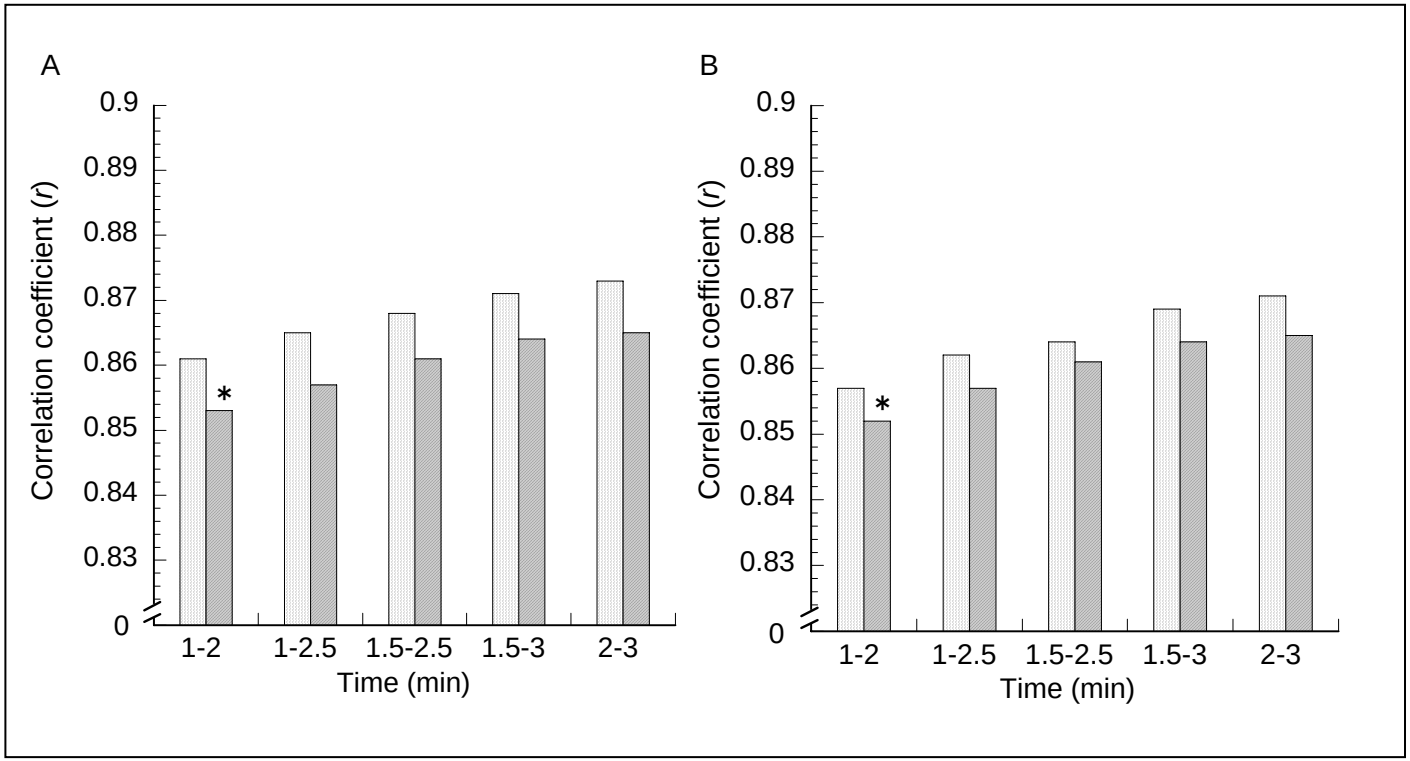
A
B
Correlation coefficient (r)
0.9
0.89
0.88
0.87
0.86
0.85
0.84
0.83
0
*
1-2
1-2.5
1.5-2.5
1.5-3
2-3
Time (min)

Figure 4

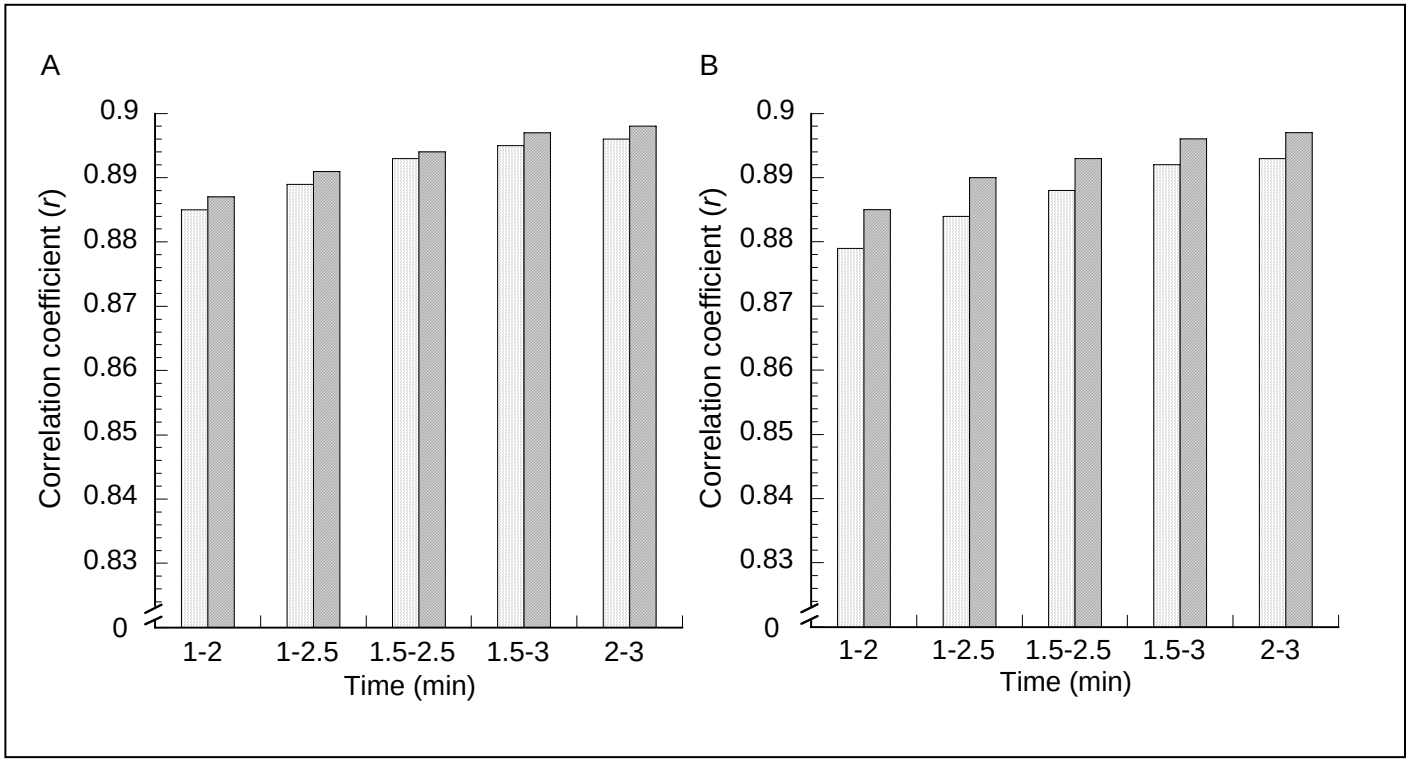
A
B
Correlation coefficient (r)
0.9
0.89
0.88
0.87
0.86
0.85
0.84
0.83
0
1-2
1-2.5
1.5-2.5
1.5-3
2-3
Time (min)

Figure 5

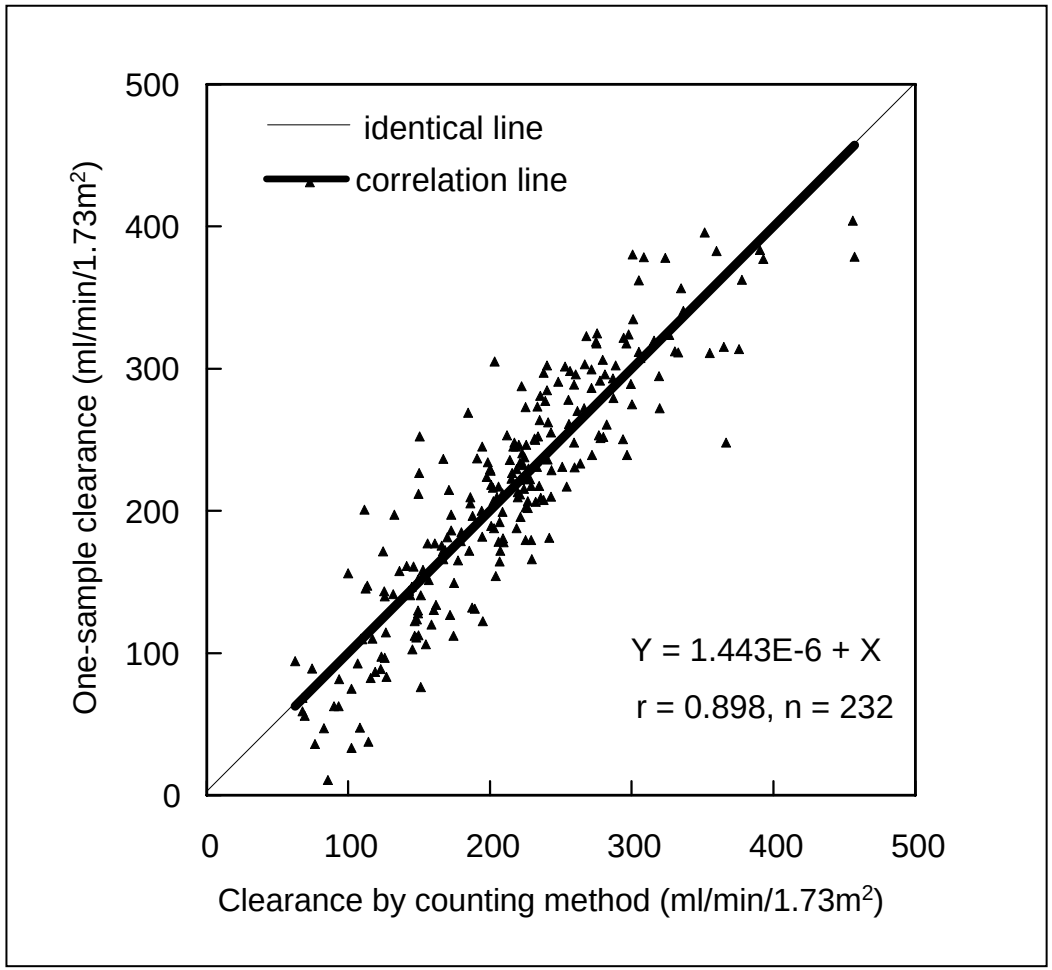
identical line
correlation line
Y = 1.443E-6 + X
r = 0.898, n = 232
One-sample clearance (ml/min/1.73m2)
Clearance by counting method (ml/min/1.73m2)
0
100
200
300
400
500

Figure 6