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Overall Accuracy of Technetium-99m-MAG3 Clearance Measurements Obtained with a Gamma Camera Heart Curve

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The aim of the present study was to evaluate the accuracy of ^{99m}Tc-MAG3 clearance measurements using a precordial gamma camera curve calibrated by a single plasma sample. **Methods:** Technetium-99m-MAG3 was administered to ten young normal volunteers. A 60-min gamma camera acquisition was performed. Five different segments of the gamma camera curve were determined: 3 min to 20 min, 3 min to 30 min, 3 min to 40 min, 3 min to 50 min and 3 min to 60 min. A biexponential function was fitted on each of these five different segments, which were thereafter calibrated using eight different blood samples. These blood samples were successively used for calibration at 5, 10, 15, 20, 30, 40, 50 and 60 min. The single injection, multiple plasma sample method was used as reference. **Results:** Camera clearances varied markedly based on the length of the precordial curve and on the time of the calibration sample. Different regression equations were obtained for each duration of the camera curve, and for each blood sample timing. Correlation coefficients were >0.95 in most cases recording period of at least 50 min, however, was necessary to obtain a s.e.e. better than those obtained using a single blood sample method without gamma camera curve. **Conclusion:** The ^{99m}Tc-MAG3 clearance determination using a gamma camera heart curve calibrated with a single blood sample does not necessarily improve the accuracy of the one blood sample method.

Key Words: technetium-99m-MAG3; gamma camera; renal clearance

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Reference methods that allow calculation of the global renal clearance include the continuous infusion method and the single injection, multiple plasma sample method. In clinical practice, simplified methods using one or fewer blood samples are more often used (*1–7*). Reduction in the number of blood samples, however, often accounts for a reduced accuracy; for example,

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TABLE 1
Comparison between Camera and Reference Clearances: Mean Difference and Probability Values (Paired t-Test)

Gamma camera curve duration (min)	Time of calibration sample (min)							
	5	10	15	20	30	40	50	60
20	40.67	61.85	88.21	96.92	64.90	11.30	−36.39	−73.34
	p = 0.044	p = 0.003	p = 0.000	p = 0.000	p = 0.000	p = 0.564	p = 0.191	p = 0.038
30	12.05	30.25	58.18	77.46	75.60	45.11	9.96	−22.12
	p = 0.205	p = 0.013	p = 0.003	p = 0.002	p = 0.002	p = 0.003	p = 0.175	p = 0.009
40	9.63	26.72	53.22	73.97	81.29	60.23	31.11	1.93
	p = 0.126	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.783
50	3.69	20.07	43.81	63.46	75.17	61.60	39.10	15.07
	p = 0.586	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.009
60	−1.95	14.40	36.20	54.41	67.53	58.75	41.59	22.42
	p = 0.773	p = 0.001	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.000	p = 0.001

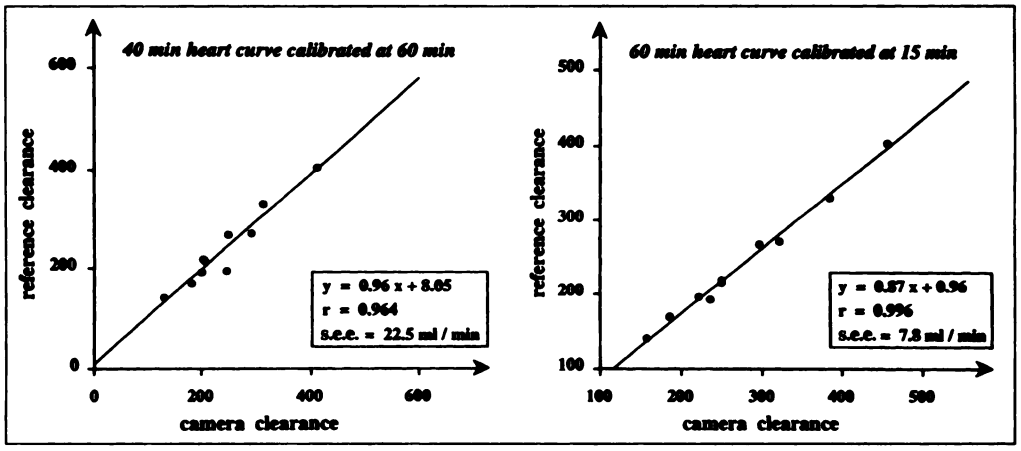

FIGURE 1. Examples of regression equations between camera clearance and reference (multiple blood sample) clearance. (Left) 40-min heart curve calibrated using the 60-min blood sample. (Right) 60-min heart curve calibrated using the 15-min blood sample. Regression equations, correlation coefficients (r) and standard errors of the estimate (s.e.e.) are different.

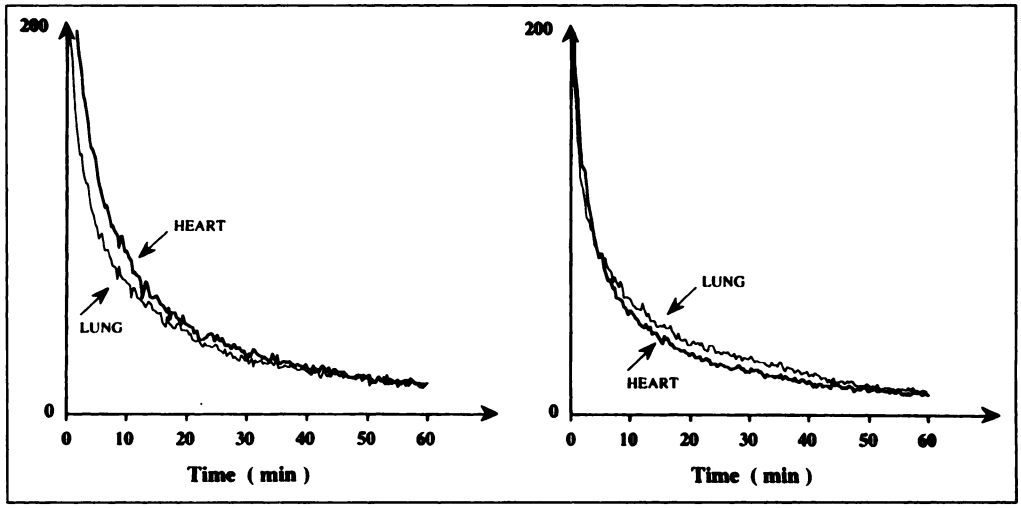

FIGURE 2. In Patient 1 (left), heart activity is higher than lung activity. Therefore a subtraction can be made. In Patient 2 (right), lung activity is higher than cardiac activity and does not allow such a correction. Failure of this correction procedure may be related to anatomical factors; indeed, the heart activity could be more or less absorbed by the osseous structures of the spine, depending on its position and orientation in the chest.

the error on the ^{99m}Tc-mercapto acetyl triglycine (MAG3) calculated clearance is about twice as large if one blood sample is used instead of two (*8–9*). Some authors have suggested that a gamma camera heart curve calibrated by means of a single blood sample could be used (*10*).

The present study was undertaken to evaluate the accuracy of the ^{99m}Tc-MAG3 clearance determinations obtained by using a gamma camera heart curve calibrated with a single blood sample. The reference method chosen for this purpose was the single injection, multiple blood sample clearance.

MATERIALS AND METHODS

Ten healthy adult volunteers, aged 21 to 34 yr (mean age: 26.3 yr) were selected. None had a remarkable medical history and none were on any medication; blood pressure was normal in all patients.

Technetium-99m-MAG3 was prepared using a freshly eluted technetium solution, according to the manufacturer's instructions (Mallinckrodt, Petten, The Netherlands). The dose, containing 185 MBq ^{99m}Tc-MAG3, and an aliquot of the dose (standard) prepared with about 44 MBq ^{99m}Tc-MAG3, were weighed. The weighing system was accurate to within 0.1 mg.

TABLE 2
Regression Equations, Correlation Coefficients (r) and s.e.e.

Gamma camera curve duration (min)	Time of Calibration Sample (min)			
	5	10	15	20
20	y = 0.72 x + 37.11 r = 0.780 s.e.e. = 52.8	y = 0.70 x + 29.20 r = 0.879 s.e.e. = 40.2	y = 0.65 x + 25.99 r = 0.927 s.e.e. = 31.7	y = 0.67 x + 13.79 r = 0.949 s.e.e. = 26.7
30	y = 0.95 x + 0.47 r = 0.938 s.e.e. = 29.3	y = 0.80 x + 23.53 r = 0.950 s.e.e. = 26.4	y = 0.67 x + 39.43 r = 0.936 s.e.e. = 29.7	y = 0.61 x + 46.45 r = 0.922 s.e.e. = 32.7
40	y = 1.14 x − 44.56 r = 0.981 s.e.e. = 16.2	y = 0.95 x − 12.62 r = 0.991 s.e.e. = 11.3	y = 0.82 x + 1.07 r = 0.987 s.e.e. = 13.6	y = 0.72 x + 3.73 r = 0.981 s.e.e. = 16.5
50	y = 1.16 x − 43.49 r = 0.975 s.e.e. = 18.7	y = 0.98 x − 14.65 r = 0.993 s.e.e. = 10.2	y = 0.86 × 3.10 r = 0.996 s.e.e. = 8.0	y = 0.80 x − 2.25 r = 0.993 s.e.e. = 9.9
60	y = 1.17 x − 38.61 r = 0.976 s.e.e. = 18.4	y = 0.99 x − 10.68 r = 0.993 s.e.e. = 10.1	y = 0.87 x + 0.96 r = 0.996 s.e.e. = 7.8	y = 0.81 x + 1.82 r = 0.994 s.e.e. = 9.3

Gamma camera curve duration (min)	Time of Calibration Sample (min)			
	30	40	50	60
20	y = 0.79 x − 1.09 r = 0.923 s.e.e. = 32.4	y = 0.69 x + 67.30 r = 0.742 s.e.e. = 56.6	y = 0.48 x + 142.37 r = 0.538 s.e.e. = 71.1	y = 0.34 x + 183.64 r = 0.399 s.e.e. = 77.3
30	y = 0.63 x + 41.57 r = 0.920 s.e.e. = 33.1	y = 0.75 x + 26.53 r = 0.945 s.e.e. = 27.5	y = 0.90 x + 14.56 r = 0.969 s.e.e. = 20.9	y = 1.03 x + 15.48 r = 0.965 s.e.e. = 22.0
40	y = 0.77 x − 7.53 r = 0.982 s.e.e. = 15.7	y = 0.85 x − 15.12 r = 0.988 s.e.e. = 13.0	y = 0.92 x − 8.00 r = 0.981 s.e.e. = 16.4	y = 0.96 x + 8.05 r = 0.964 s.e.e. = 22.5
50	y = 0.80 x − 12.72 r = 0.991 s.e.e. = 11.5	y = 0.85 x − 16.98 r = 0.990 s.e.e. = 12.1	y = 0.90 x − 10.71 r = 0.987 s.e.e. = 13.4	y = 0.94 x + 0.38 r = 0.985 s.e.e. = 14.4
60	y = 0.81 x − 8.65 r = 0.992 s.e.e. = 10.8	y = 0.85 x − 14.01 r = 0.992 s.e.e. = 10.7	y = 0.89 x − 9.53 = 0.991 s.e.e. = 11.4	y = 0.91 x + 0.06 r = 0.989 s.e.e. = 12.3

x = gamma camera clearance; y = reference clearance.
Clearance and s.e.e. are given in ml/min.

Patients lay in the supine position on a plexiglass bed with the gamma camera underneath; the heart and the kidneys were included in the field of view. Acquisition was started immediately after tracer injection; 180 frames, of 20 sec each, were recorded in a 64 × 64 matrix using a large field of view gamma camera equipped with an all-purpose collimator.

To rule out locally remaining radioactivity, a 1-min frame was acquired on the injection site after the end of the recording period. The empty syringe and the standard were counted twice in similar conditions on the camera; the ratio of these two measurements was used to estimate the weight of the residue.

Eleven blood samples were taken at 5, 10, 15, 20, 25, 30, 40, 50, 60, 90 and 120 min from the arm opposite to that used for tracer injection. The serum samples and a dilution of the standard were counted in a well scintillator. The reference clearance (multiple blood sample method) was obtained by applying a biexponential function on the experimental plasma curve (*11*). A heart curve was generated by delineating a region of interest (ROI) over the left ventricle. Gamma camera clearance calculation was performed using a segment of the camera heart curve. A biexponential function was fitted on this curve, which was thereafter calibrated using one blood sample. Five different segments (3 to 20, 3 to 30, 3 to 40, 3 to 50 and 3 to 60 min) were chosen, and eight different blood samples (5, 10, 15, 20, 30, 40, 50 and 60 min) were successively used for calibration. These procedures allowed us to obtain 40 different gamma camera clearance estimations for each subject.

Technetium-99m-MAG3 clearance was also calculated according to Russell's single sample algorithm (*8*), using the 40- and 50-min blood samples. Clearance values were expressed in ml/min, without body surface area correction.

The gamma camera clearance was compared to the reference clearance using a paired t-test; gamma camera clearances and the single blood sample clearances calculated according to Russell's algorithm were compared to the reference clearance using simple linear regression analysis.

RESULTS

For all subjects, gamma camera clearance values were different from those of the reference clearances. They also varied markedly according to the length of the precordial curve and the time of the calibration sample. Differences between the camera and reference clearances are summarized in Table 1. The p values (paired t-test) are also presented. In most of the

TABLE 3
Comparison between Russell's Single-Sample Clearance and Reference Clearance

Single-sample method	Correlation coefficient	s.e.e.
Sampling time = 40 min	0.976	19.6 ml/min
Sampling time = 50 min	0.982	16.1 ml/min

cases, the camera method overestimated the reference clearance.

The results of the linear regression analysis [regression equations, correlation coefficients (r) and standard errors of the estimate (s.e.e.)] are shown in Table 2. With the exception of the 20-min precordial curves, correlation coefficients were always higher than 0.90; in most of the cases, these coefficients were higher than 0.95. Regression equations, however, differed for each of the 40 camera clearance measurements (Table 2, Fig. 1). A large range of s.e.e. (20.9 ml/min–77.3 ml/min) was observed for the 20 and 30 min acquisitions; s.e.e. values inferior to 10 ml/min were only obtained for acquisitions of at least equal to 50 min.

Table 3 summarizes the correlation coefficients and s.e.e. measurements obtained with Russell's single-sample algorithm and the reference method: these s.e.e. were less than 20 ml/min for plasma samples taken 40 and 50 min after tracer injection. With a gamma camera heart curve calibrated by means of a single blood sample, such s.e.e. measurements were obtained only when the recording times were at least 40 min.

DISCUSSION

Technetium-99m-MAG3 was introduced several years ago as a comparatively advantageous renal radiotracer when compared to other available renal agents, such as OIH and DTPA (*12–17*). Several algorithms that require few blood samples and allow global ^{99m}Tc-MAG3 clearance rates to be calculated have been published (*7–9,18–20*). The accuracy of these methods, however, depends on the number of blood samples both in adults (*8*) and in children (*9*). In 1991, Gordon et al. (*10*) found an excellent correlation between the multiple blood sample method and the method using a gamma camera heart curve calibrated with a single blood sample.

In the present study, we also obtained correlation coefficients higher than 0.90. Satisfactory correlation coefficients, however, do not necessarily attest to the accuracy of the method. Indeed, a recording period of at least 40 min was necessary to obtain s.e.e. similar to those obtained using the single blood sample calculation. Moreover, to obtain a s.e.e. value less than 10 ml/min, a recording time of at least 50 min was required.

Although an underestimation was sometimes observed, the ^{99m}Tc-MAG3 clearance rates calculated from gamma camera heart curves were overestimated in most of the cases. It has previously been shown that the precordial curve does not reflect the plasmatic disappearance curve accurately, when using ^{99m}Tc-MAG3, probably because the precordial ROI includes an extravascular compartment (*21–22*). For rapidly cleared tracers, such as ^{99m}Tc-MAG3, the late extravascular concentration is relatively high compared to the low plasmatic concentration (*21*). Some authors (*22–23*) have argued for corrections to this interstitial component. We tried to make such a correction by generating an extravascular time-activity curve obtained from a ROI drawn over the lung; this extravascular curve was further subtracted from the heart curve. While this procedure seems theoretically attractive, the correction was not feasible in some cases (Fig. 2).

Besides errors caused by interstitial diffusion, short camera curve durations can also induce erroneous renal clearance calculations due to incorrect estimation of the second exponential. Depending on the time chosen to calibrate the curve by a plasma sample, this error can lead to an over or underestimation of the clearance value.

CONCLUSION

Technetium-99m-MAG3 clearance values determined with a gamma camera heart curve calibrated by means of a single plasma sample do not always improve the single blood sample method. Better results are obtained only with acquisition periods of at least 50 min.

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