
Effective Renal Plasma Flow Determination Using Technetium-99m MAG₃: Comparison of Two Camera Techniques with the Tauxe Method

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Previous studies have suggested that by slight modification of the current formulas for iodine-131 (¹³¹I) orthoiodohippurate (OIH) effective renal plasma flow (ERPF) quantitation, technetium-99m (^{99m}Tc) mercaptoacetyl triglycine (MAG₃) can be substituted for ¹³¹I-OIH in the quantitative renal function protocol. This study was undertaken to compare two different camera techniques that do not require blood samples. The Schlegel camera method, modified by the introduction of 0.67 as a correction factor, comprised one technique. In the other technique, the renal clearance (RC) was determined and then converted to ERPF. The results were then compared with the Tauxe (TX) method. Fifty patients with varying degrees of renal impairment were studied. Our comparative results support the concept that a camera technique can be applied to ^{99m}Tc-MAG₃ to determine ERPF, with results similar to those obtained by the Tauxe method ($p < 0.01$).

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The gold standard for the measurement of renal function is the classical paraaminohippuric acid (PAH) continuous infusion technique, and its clearance is a measure of effective renal plasma flow (ERPF). However, it is not well suited for routine clinical studies (1,2). Such determination of ERPF has been greatly simplified by the use of regression equations, based on a single plasma activity measurement of iodine-131 (¹³¹I) orthoiodohippurate (OIH) 44 min postinjection (3). Recently, technetium-99m (^{99m}Tc) mercaptoacetyl triglycine (MAG₃) has become commercially available for routine clinical use in the U.S. and has been proposed as a suitable replacement for ¹³¹I-OIH (4-6). This agent combines a rapid kidney uptake, similar to that achieved with ¹³¹I-OIH, with the favorable imaging properties of ^{99m}Tc (7).

Since the clearance of ^{99m}Tc-MAG₃ correlates strongly with that of ¹³¹I-OIH, it can be used as an independent measure of renal function (8-15). It should be noted that unlike hippuran, only a small component of ^{99m}Tc-MAG₃ is cleared by glomerular filtration. With slight modification of the current ¹³¹I-OIH formulas for determining ERPF, it can be estimated from ^{99m}Tc-MAG₃ clearance, by substituting the corrected ^{99m}Tc-MAG₃ activity for ¹³¹I-OIH in the quantitative protocol. This use of ^{99m}Tc-MAG₃ for imaging also results in better image quality and lower radiation dose to patients who have decreased renal function (11).

The purpose of this study was to compare two different camera techniques not requiring blood samples, with the modified Tauxe method (1-blood sample) for quantitating ERPF with ^{99m}Tc-MAG₃, and to determine if either served as a suitable and simplified way of determining ERPF with ^{99m}Tc-MAG₃.

MATERIALS AND METHODS

A large field of view camera (Elscent 409 Mobile, Elscint, Hackensack, NJ), fitted with a low energy, medium resolution, medium sensitivity collimator was used. All patients were injected intravenously with 2 to 2.5 mCi of ^{99m}Tc-MAG₃ (Mallinckrodt, St. Louis, MO), through a butterfly infusion set to avoid infiltration on those subjects who have small or fragile veins. The dose in the syringe was counted for 1 min in a phantom holder at a distance of 30 cm from the collimator face, immediately prior to and following the study. Data were acquired in a dynamic mode at 2 sec/frame for 120 sec, followed by 15 sec/frame for 28 min.

The calculation of ERPF for the first camera technique was done according to the current commercially available Schlegel program (16), which was modified by the introduction of 0.67 as a correction factor (17). Using the second camera technique, renal clearance was determined (18) according to the formula:

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$$\text{Clearance (ml/min)} = 824.2X - 8.04,$$

where X equals the background and attenuation-corrected renal counts at 2–3 min postinjection, divided by the injected dose (cts/min). This figure was then converted to ERPF, for the purpose of comparison with normal values listed in the literature (14,19).

$$\text{ERPF (ml/min)} = 1.818 \times C + 22.9,$$

where C equals clearance in ml/min.

The Tauxe method involved the preparation of standards and the drawing of a plasma sample at ~45 min postinjection (20,21). Data analysis was performed using the Student's t-test. A value of $p < 0.01$ was considered highly significant. Conventional regression analysis was used to obtain the correlation coefficient (r), and the coefficient of determination (r^2). The estimated ERPF was plotted using linear regression.

RESULTS

Table 1 lists the global ERPF values from all three modalities; these values were not significantly different from one another ($p < 0.01$). The correlation coefficients obtained were highly significant. Comparisons were made between the modified Schlegel camera technique (MSC) and the Tauxe method (TX) ($r = 0.9673$); between the renal clearance camera technique (RC) and TX ($r = 0.9609$), and between the two camera techniques, RC and MSC ($r = 0.9688$).

The graphs of estimated ERPF via linear regression among all comparisons are shown in Figures 1, 2, and 3.

DISCUSSION

ERPF is a measure of renal function, an important parameter that helps to clarify the nature of many kidney disorders; much like glomerular filtration rate or creatinine clearance, it can be used to evaluate function and monitor changes (2,3,7).

The tedious method of continuous PAH infusion to measure tubular cell function has been greatly simplified by the use of regression equations, based on the injected dose and the reciprocal of the plasma activity at a predetermined time postinjection (3,11). However, this single-sample procedure is technically demanding, since it requires meticulous and careful attention to detail, in order to obtain accurate results. Attention must be paid to making sure infiltration is excluded; drawing the plasma sample from an area other than the injection site; not overloading the well counter; and most important, the careful pipetting in making the dilutions necessary for the preparation of standards (8).

Although simplified techniques, requiring only monthly preparation of standards, have been described in the literature for ^{131}I -OIH (21,22), they cannot be applied to a $^{99\text{m}}\text{Tc}$ -based compound. Therefore, there is a high possibility of error associated with repeated preparation of standards. The correction factor (MAG₃/OIH clearance ratio) needed in

TABLE 1. Global ERPF Values for MAG₃ (ml/min)

Patient #	Camera Method (0.67)	Tauxe Method (blood sample)	Clearance Method
1	234	303	217
2	402	388	416
3	247	263	230
4	372	406	377
5	337	364	275
6	241	204	196
7	184	143	165
8	143	119	130
9	326	407	333
10	200	178	212
11	299	229	246
12	576	625	592
13	137	153	118
14	382	368	329
15	136	126	118
16	93	83	89
17	333	354	266
18	427	427	447
19	154	145	101
20	538	554	532
21	695	616	633
22	199	167	163
23	266	275	233
24	203	171	217
25	194	188	213
26	294	382	322
27	389	323	329
28	446	476	440
29	378	393	411
30	151	192	130
31	328	392	352
32	112	119	129
33	364	304	335
34	417	434	402
35	248	239	215
36	409	458	409
37	442	441	493
38	83	88	72
39	615	597	579
40	397	341	341
41	115	138	157
42	212	214	189
43	390	384	301
44	442	438	381
45	66	73	88
46	255	249	212
47	475	479	553
48	281	296	215
49	388	437	352
50	373	347	309

Referring diagnosis and number of patients: renal artery stenosis (5), hypertension (5), renal insufficiency (7), hematuria (5), pyelonephritis (3), hydronephrosis (3), obstruction (5), renal failure (3), trauma (2), proteinuria (2), diabetes (3), flank pain (3), kidney stones (4). Age: 16 to 80 yr, BUN: 7.0 to 140 mg/dl, creatinine: 0.7 to 10.7 mg/dl, ERPF: 66 to 695 ml/min, single kidney: 6 pts. (native kidney), M = 19, F = 31.

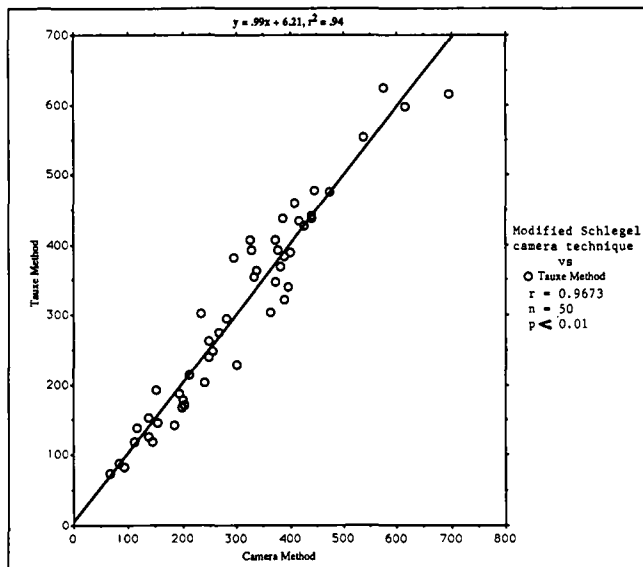


FIG. 1. Correlation between the ERPF estimated from the modified Schlegel camera technique (MSC) and that from the Tauxe (1-blood sample) method (TX).

the modified Tauxe formulas that have been adapted for $^{99m}\text{Tc-MAG}_3$ (11) has varied from a value as low as 0.47 to one as high as 0.714 (see Table 2).

It has been suggested that such differences in the clearance ratio are due to the variations in the radiochemical purity or the different sources of the labeling kit (or even on the patient's diagnosis, although the available data do not support this). However, these differences have not been found to affect the percentage of plasma protein binding (1, 13, 14, 23). It is also argued in the literature that impurities are not the significant factor; but rather, the differences in the clearance ratio are due to the methodological differences

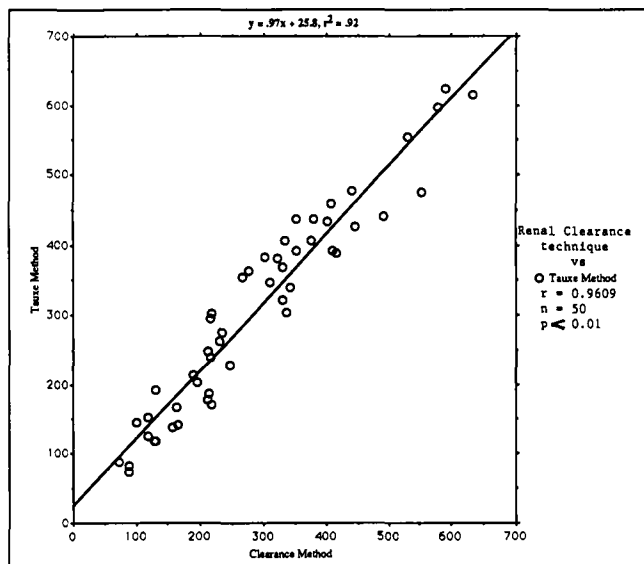


FIG. 2. Correlation between the ERPF estimated from the renal clearance technique (RC) and that from the Tauxe (1-blood sample) method (TX).

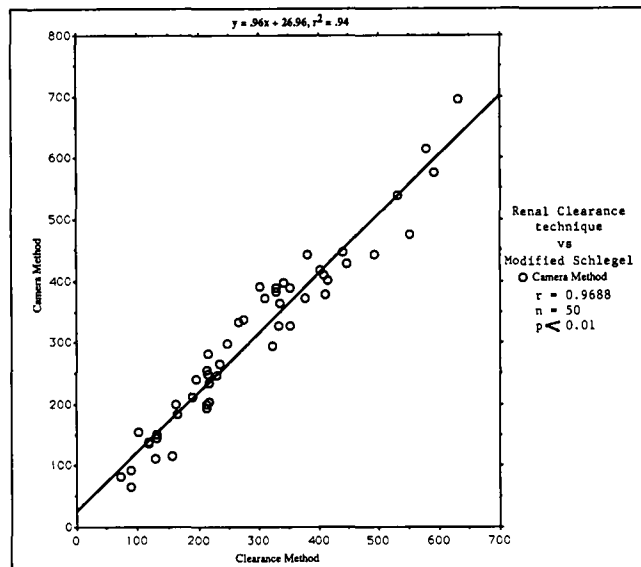


FIG. 3. Correlation between the ERPF estimated from the renal clearance technique (RC) and that from the modified Schlegel camera technique (MSC).

in determining the ratio (24,25). The cause of the discrepancy is still unclear and needs to be resolved.

The correction factor to modify the Schlegel camera program in this laboratory was 0.67 (17). We felt that in order to maintain consistency in our study, the same correction factor should be used to modify the Tauxe protocol.

Calculation of ERPF by the camera method alone has two distinct advantages: no blood sample is necessary and no laborious preparation of standards is required. Although the in vitro method of ERPF determination is more accurate, and the accuracy of the technique using the camera alone has been questioned (26), the absolute values of ERPF in individual patients may not be of great importance. Rather, it is the actual changes on serial studies that are of great importance as indicators of pathology. The value of an accurate quantitative determination, such as with the in vitro ERPF method, is greatly reduced whenever there is no baseline

TABLE 2. MAG_3 Clearance Data from the Literature

Reference #	MAG_3/OIH Clearance Ratio
6	0.61
7	0.56
10	0.56, 0.57
11	0.563, 0.57
12	0.57, 0.70
13	0.66, 0.67
14	0.55–0.714
15	0.51
19	0.51
24	0.47
28	0.53, 0.59, 0.62
29	0.62

measurement in the patient's record. Arguably then, the value of renal function quantitation lies in its consistency and in the availability of a baseline measurement for each patient, allowing the detection of changes in renal function, as it is determined in successive follow-up procedures (25,27).

It has also been proposed that the Schlegel technique may not be a suitable camera method for ^{99m}Tc -MAG₃, since no attenuation factor for ^{131}I -OIH was included in the calculation. This factor was apparently assumed to equal the square of the kidney depth. The depth correction factor for ^{131}I -OIH will be different than that for ^{123}I -OIH, and will also be different than that used for ^{99m}Tc -MAG₃. Moreover, the Schlegel technique would be valid only if ^{99m}Tc -MAG₃ and ^{131}I -OIH had identical volumes of distribution (19,30,31). As has been demonstrated in previous studies, the volume of distribution for ^{99m}Tc -MAG₃ is less than that of ^{131}I -OIH (1,5,6,13,19,24).

Due to these limitations, the Schlegel technique may not give accurate results, and there is the possibility that it might fail in certain disease states (25), such as nephrotoxicity, sickle cell disease, pediatric diseases, and renal transplants (32). Considering the limitations of the Schlegel technique, the renal clearance technique may be a better camera method.

No renal transplant studies were included in our study, due to the lack of an adequate sample number. There might be a simpler method of determining the renal clearance on such patients using only the camera, and then converting the value to an ERPF. The premise of the camera-only technique is that the background activity at the 25th min postinjection should be inversely proportional to clearance, since ^{99m}Tc -MAG₃ is highly protein bound and tends to stay within the intravascular compartment (33).

CONCLUSION

The present study sought to investigate the clinical value of a camera-based methodology for the quantitation of ERPF. The results from the three modalities were not significantly different. Therefore, based on the data derived from this specific study, and within the limitations and assumptions underlying this study, these comparative results support the concept that a camera clearance technique can be applied to determine ERPF with ^{99m}Tc -MAG₃ ($p < 0.01$).

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REFERENCES

1. Eshima D and Taylor A. Technetium-99m (^{99m}Tc) mercaptoacetyltriglycine: update on new ^{99m}Tc renal tubular function agent. *Semin Nucl Med* 1992;22:61-73.
2. Tauxe WN and Dubovsky EV. *Nuclear medicine in clinical urology and nephrology*. Norwalk CT: Appleton-Century-Crofts; 1985:61-105.

3. Tauxe WN, Dubovsky EV, Kidd T, et al. New formulas for the calculation of effective renal plasma flow. *Eur J Nucl Med* 1982;7:51-54.
4. Fritzberg A, Kasina S, Eshima D, et al. Synthesis and biological evaluation of technetium-99m MAG₃ as a hippuran replacement. *J Nucl Med* 1986;27:111-116.
5. Taylor A, Eshima D, Fritzberg A, et al. Comparison of iodine-131 OIH and technetium-99m MAG₃ renal imaging in volunteers. *J Nucl Med* 1986;27:795-803.
6. Jaffri RA, Britton KE, Nimmon CC, et al. Technetium-99m MAG₃: a comparison with iodine-123 and iodine-131 orthoiodohippurate in patients with renal disorders. *J Nucl Med* 1988;29:147-158.
7. Russell CD, Young D, Billingsley JD, et al. Technical procedures for use of the new kidney agent technetium-99m MAG₃. *J Nucl Med Technol* 1991;19:147-152.
8. Taylor A, Corrigan P, Eshima D, et al. Prospective validation of a single sample technique to determine technetium-99m MAG₃ clearance. *J Nucl Med* 1992;33:1620-1622.
9. Bubeck B, Brandau W, Steinbacher M, et al. Technetium-99m-labeled renal functions and imaging agents. Clinical evaluation of ^{99m}Tc -MAG₃ (^{99m}Tc -mercaptoacetylglucyl-glycylglycine). *Nucl Med Biol* 1988;15:109-118.
10. Russell CD, Thorstad B, Yester MV, et al. Comparison of technetium-99m MAG₃ with iodine-131 hippuran by a simultaneous dual channel technique. *J Nucl Med* 1988;29:1189-1193.
11. Russell CD, Thorstad B, Yester MV, et al. Quantitation of renal function with technetium-99m MAG₃. *J Nucl Med* 1988;29:1931-1933.
12. Taylor A, Eshima D, Christian PE, et al. Technetium-99m MAG₃ kit formulation: preliminary results in normal volunteers and patients with renal failure. *J Nucl Med* 1988;29:616-622.
13. Bubeck B, Brandau W, Weber E, et al. Pharmacokinetics of technetium-99m-MAG₃ in humans. *J Nucl Med* 1990;31:1285-1293.
14. Muller-Suur R, Magnusson G, Bois-Svensson I, et al. Estimation of technetium-99m mercaptoacetyltriglycine plasma clearance by use of one single plasma sample. *Eur J Nucl Med* 1991;18:28-31.
15. Muller-Suur R, Bois-Svensson I, and Mesko L. A comparative study of renal scintigraphy and clearance with technetium-99m-MAG₃ and iodine-123 hippurate in patients with renal disorders. *J Nucl Med* 1990;31:1811-1817.
16. Schlegel JU, Halikiopoulos HL, and Prima R. Determination of filtration fraction using the gamma scintillation camera. *J Urol* 1979;122:447-450.
17. Arroyo A, Comparison of technetium-99m-MAG₃ and iodine-131 OIH ERPF results using the camera technique. *J Nucl Med Technol* 1991;19:173-175.
18. Taylor A, Halkar RK, Garcia E, et al. A camera-based method to calculate ^{99m}Tc -MAG₃ clearance. (Abstract.) *J Nucl Med* 1991;32:953.
19. Taylor A, Siffer JA, Steves A, et al. Clinical comparison of I-131 orthoiodohippurate and the kit formulation of ^{99m}Tc -mercaptoacetyltriglycine. *Radiology* 1989;170:721-725.
20. Tauxe NW, Maher FT, and Taylor WF. Effective renal plasma flow: estimation from theoretical volumes of distribution of intravenously injected I-131 orthoiodohippurate. *Mayo Clin Proc* 1971;46:524-531.
21. Sirota PS, Brust K, and Nelp WB. Preparation of standards for the calculation of effective renal plasma flow. *J Nucl Med Technol* 1986;14:132-134.
22. Floyd JL, Jackson DE, and Thomas JM. A simplified method for the routine determination of effective renal plasma flow. *Clin Nucl Med* 1986;11:758-759.
23. Russell CD, Taylor A, and Eshima D. Estimation of technetium-99m-MAG₃ plasma clearance in adults from one or two blood samples. *J Nucl Med* 1989;30:1955-1959.
24. Prenen JA, Klerk JMH, van het Schip AD, et al. Technetium-99m-MAG₃ versus iodine-123-OIH: renal clearance and distribution volume as measured by a constant infusion technique. *J Nucl Med* 1991;32:2057-2060.
25. Russell CD, and Dubovsky EV. Editorial: quantitation of renal function using MAG₃. *J Nucl Med* 1991;32:2061-2062.
26. Fine EJ, Axelrod M, Gorkin J, et al. Measurement of effective renal plasma flow: a comparison of methods. *J Nucl Med* 1987;28:1393-1400.

27. Eggli D. Renal imaging and ERPF determination: better, faster, easier. *Mallinckrodt Medical* 1991;1:1–6.
28. Kengen RA, Meijer S, Beekhuis H, et al. Technetium-99m-MAG₃ clearance as a parameter of effective renal plasma flow in patients with proteinuria and lowered serum albumin levels. *J Nucl Med* 1991;32:1709–1712.
29. Keske U, Cordes M, Wilfling M, et al. Comparison of Tc-99m-MAG₃ and I-131 OIH in patients with normal and impaired renal function. (Abstract.) *Clin Nucl Med* 1989;14:P18.
30. Taylor A, and Datz FL. *Clinical practice of nuclear medicine*. New York: Churchill Livingstone; 1991:121–124.
31. Taylor A and Eshima D. Effects of altered physiologic states on clearance and biodistribution of technetium-99m MAG₃, iodine-131 OIH, and iodine-125 iothalamate. *J Nucl Med* 1988;29:669–675.
32. Blaufox MD. *Evaluation of renal function and disease with radionuclides*, 2nd ed. Basel, Switzerland: S. Karger, A. G.; 1989:150–184.
33. Halkar RK, Galt J, and Taylor A. A new gamma camera method to determine Tc-99m MAG₃ clearance in renal transplant patients. (Abstract.) *J Nucl Med* 1991;32:953.