Off-Site Determinations of Effective Renal Plasma Flow Using Technetium-99m-MAG3 and Single Blood Sampling

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This study evaluated the feasibility of determining effective renal plasma flow (ERPF) at an off-site central laboratory by transferring blood samples from the on-site laboratory.

Methods: Blood samples were obtained from 66 patients referred for renal imaging with ^{99m}Tc-MAG3. ERPF values were determined using the single blood sample method (BSM) at both on- and off-site laboratories. The ERPF values were classified clinically as normal or abnormal. Both the ERPF values and clinical classification were compared between on- and off-site laboratories.

Results: The off-site ERPF overestimated those on-site by 2.8% (paired Student's t-test $p < 10^{-5}$). However, off-site ERPF values highly correlated with the values obtained on-site ($r = 0.99$; $p < 10^{-5}$). In addition, the clinical classification for each patient determined at each site was identical.

Conclusion: ERPF can be determined accurately off-site. This method should allow many nuclear medicine departments access to the ERPF determination by the BSM at a central off-site laboratory.

Key Words: technetium-99m-MAG3; effective renal plasma flow; kidney; renal function

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Effective renal plasma flow (ERPF) is a quantitative measure of renal function (*1*). The single blood sample method (BSM) described by Tauxe (*2*) for calculation of ERPF with orthoiodohippurate (OIH) is well established. This calculation can be modified for use with technetium-99m-mercaptoacetyltriglycine (MAG3; Mallinckrodt, Inc., St. Louis, MO) by introducing a correction factor, which is actually a clearance ratio, MAG3/OIH (*3–5*). The correction factor used in this study was 0.61. The major advantage of measuring renal function by ERPF as compared to glomerular filtration rate (GFR) is that ERPF can be measured in a shorter period of time. A 44-min blood sample as opposed to 180–240 min for GFR (*6–9*).

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BSM has been shown to be more accurate than the gamma camera methods for renal function measurements (*9–13*). The camera methods have many steps where errors can be introduced, such as renal depth correction (*14,15*) and background correction for obtaining the true renal time-activity curve (*16,17*). The errors associated with these steps thus lower the accuracy of the ERPF result (*18,19*). Although BSM is free of these errors, it is time consuming, requiring quantitative laboratory skills in preparing standards (*6,13*). Thus, BSM may not be suited for all nuclear medicine departments. This study compared the ERPF results calculated at both an on- and an off-site laboratory and sought to determine if the off-site results were acceptable.

MATERIALS AND METHODS

Renal imaging was performed on 66 patients with varying histories and degrees of renal function. Patients were injected intravenously with 220–260 MBq (6–7 mCi) ^{99m}Tc-MAG3, measured in dose calibrators both off-site and on-site. Exact measurement times were recorded for each and a dose calibrator correction factor (DCCF) was determined. After injection for the renal scan (on-site), the dose syringe and injection apparatus were reassayed. The residual activity and time were recorded, then the net injected dose on-site was determined. When the renal scan was completed (21 min), an image of the injection site was obtained on all patients to evaluate any possible partial interstitial injections.

A 10-ml blood sample was collected in a heparinized tube 44 min after injection, from the contralateral arm. This blood sample was then centrifuged (750 G for 15 min) within 1 hr on-site to obtain a plasma sample. Known standards of pertechnetate were made up on- and off-site according to the same protocol (*6*). From these standards, the number of counts/MBq was determined for each well counter (on- and off-site). Thus, the net injected patient dose was converted from MBq to counts. The standard and patient's plasma sample were counted in duplicates at the same time. This allowed calculation of Vt, the volume of distribution at the sample time and, subsequently, ERPF was determined (*1*).

The patient's plasma then was added back to the red cells and resuspended in the original blood sample tube, and sent to the off-site central laboratory, usually early the next morning. Thus, the blood sample arrived at the off-site laboratory in the same form as it was drawn on-site. At both sites, the storage of the samples was at room temperature. The blood sample was then recentrifuged to obtain plasma samples. Using the off-site known standards, the ERPF was determined using the DCCF to convert the net injected patient dose on-site to an off-site value. The time delay between injecting the ^{99m}Tc-MAG3 and counting the patient's plasma samples in the well counter at the off-site laboratory was approximately 25 hr.

Data analysis was performed by two different methods: comparison of ERPF values and clinical classification between the two sites. A Pearson correlation coefficient for the off-site ERPF values was calculated against that of the reference on-site. A paired Student's t-test was used to compare the two values to see if they were different from each other.

For clinical classification, we established for each patient the expected lower limit of normal (LLN) of the ERPF value based on age and gender by using the nomograms from Tauxe (*1*). Then the ERPF value for each patient was classified into a clinical result as normal or abnormal by comparison to the LLN for that patient. These clinical results were determined both on- and off-site for each patient and compared.

RESULTS

The ERPF values are listed in Table 1. A summary of the statistical data analysis is listed in Table 2. The paired Student's t-test indicated that the off-site ERPF overestimated the on-site by 2.8% ($p < 10^{-5}$), however, there was a significant correlation with the ERPF values performed on-site. A plot of the off-site ERPF values against those of the reference on-site is shown in Figure 1. The linear regression equation for this plot was $Y = 1.347 + 1.026 \times X$, the Pearson correlation coefficient was $r = 0.99$ ($p < 10^{-5}$). Clinical classification results of each ERPF as either normal or abnormal was identical for the on- and the off-site measurements (41 normal and 25 abnormal patients).

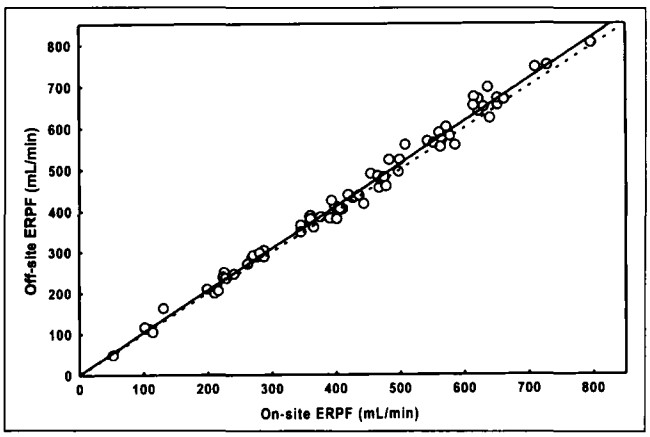

FIGURE 1. Correlation between off-site and on-site ERPF values. The solid and dotted lines represent the regression line and the line of identity with on-site ERPF values, respectively.

TABLE 1
ERPF Values for Technetium-99m-MAG3 (ml/min)

Patient #	On-site	Off-site	Patient #	On-site	Off-site
1	391	383	34	400	411
2	652	655	35	497	494
3	269	287	36	483	523
4	131	162	37	637	697
5	226	250	38	508	559
6	454	490	39	241	246
7	199	209	40	217	205
8	578	581	41	102	116
9	346	366	42	346	350
10	426	432	43	398	412
11	366	361	44	475	481
12	361	385	45	393	426
13	651	671	46	288	288
14	211	199	47	114	104
15	499	523	48	615	674
16	572	602	49	406	406
17	271	291	50	228	236
18	109	111	51	543	568
19	465	484	52	262	271
20	467	456	53	622	640
21	419	439	54	281	297
22	622	669	55	376	386
23	360	389	56	553	563
24	662	668	57	586	558
25	561	588	58	563	554
26	565	571	59	729	751
27	52	48	60	443	417
28	402	381	61	614	654
29	410	405	62	436	438
30	224	239	63	797	805
31	478	460	64	361	381
32	288	304	65	710	746
33	640	623	66	630	651

DISCUSSION

Our results demonstrate that there is a strong linear correlation between the two ERPF values. The paired Student's t-test demonstrated that there was a statistically significant difference between the two ERPF measurements on the same patient (*20*). The explanation for this overestimation of ERPF off-site is unclear. Perhaps it is due to the time delay, extra handling of the blood samples or the differences in equipment

TABLE 2
Summary Statistics for 66 Patients (men/women = 29/37)

	Mean	s.d.	Range
Age (yr)	55	16	23–85
On-site ERPF (ml/min)	427	172	52–797
Off-site ERPF (ml/min)	439	177	48–805
Difference (ml/min)	12	19	−28–60
On-site time delay* (min)	203	169	86–1330†
Off-site time delay* (min)	1523	248	1214–1784

*Time delay between injection and counting of plasma samples.
†In only one instance was the delay past 343 min (the 1330 value).

(dose calibrator and well counter). However, the mean difference of 12 ml/min ($p < 10^{-5}$) is low and within the error of the estimate for the single BSM (19 ml/min) (*12*). In addition, our clinical classification results suggest that this method can be used reliably for clinical purposes.

CONCLUSION

Our results indicate that ERPF can be determined accurately off-site by having the patient's blood sample sent out to a remote central laboratory. The average time delay between injection and counting of the plasma samples was 25.4 hr, and this still provided clinically accurate results. This will allow access to ^{99m}Tc-MAG3 ERPF determinations by the more accurate BSM to many nuclear medicine departments that do not have the current capability, or time, to perform these studies.

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REFERENCES

1. Tauxe WN, Dubovsky EV. *Nuclear medicine in clinical urology and nephrology*. Norwalk, CT: Appleton-Century-Crofts; 1985:77–90.
2. Tauxe WN, Dubovsky EV, Kidd T Jr, et al. New formulas for the calculation of effective renal plasma flow. *Eur J Nucl Med* 1982;7:51–54.
3. Russell CD, Taylor A, Eshima D. Estimation of technetium-99m-MAG3 plasma clearance in adults from one or two blood samples. *J Nucl Med* 1989;30:1955–1959.
4. 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.
5. Russell CD, Dubovsky EV. Quantitation of renal function using MAG3. *J Nucl Med* 1991;32:2061–2063.
6. 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.
7. Arroyo AJ, Burns JB, Patel YP. Derived GFR (dGFR) values from technetium-99m-MAG3 data: a comparison with the 24-hour creatinine clearance. *J Nucl Med Technol* 1996;24:223–226.
8. Rowell KL, Kontzen FN, Stutzman ME, et al. Technical aspects of a new technique for estimating glomerular filtration rate using technetium-99m-DTPA. *J Nucl Med Technol* 1986;14:196–198.
9. Blaufox MD, Aurell M, Bubeck B, et al. Report of the radionuclides in nephrourology committee on renal clearance. *J Nucl Med* 1996;37:1883–1890.
10. Dubovsky EV, Russell CD. Radionuclide evaluation of renal transplants. *Semin Nucl Med* 1988;18:181–198.
11. Taylor A, Reese L, Folks R, et al. Preliminary results of a multicenter trial to determine the clearance of technetium-99m-MAG3 by single sample and camera based techniques. *J Nucl Med* 1993;34:251P.
12. Eshima D, Taylor A Jr. Technetium-99m mercaptoacetyltriglycine: update on the new ^{99m}Tc renal tubular function agent. *Semin Nucl Med* 1992;22: 61–73.
13. Russell CD, Dubovsky EV. Measurement of renal function with radionuclides. *J Nucl Med* 1989;30:2053–2057.
14. Taylor A, Lewis C, Giacometti A, et al. Improved formulas for the estimation of renal depth in adults. *J Nucl Med* 1993;34:1766–1769.
15. Gruenewald SM, Collins LT, Fawdry RM. Kidney depth measurement and its influence on quantitation of function from gamma camera renography. *Clin Nucl Med* 1985;10:398–401.
16. Tondeur M, Piepsz A, Dobbeleir A, et al. Technetium-99m mercaptoacetyltriglycine gamma camera clearance calculations: methodological problems. *Eur J Nucl Med* 1991;18:83–86.
17. Piepsz A, Dobbeleir A, Ham HR. Effect of background correction on separate technetium-99m-DTPA renal clearance. *J Nucl Med* 1990;31:430–435.
18. 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.
19. Blaufox MD. Procedures of choice in renal nuclear medicine. *J Nucl Med* 1991;32:1301–1309.
20. Bernier DR, Christian PE, Langan JK. *Nuclear medicine technology and techniques*, 3rd ed. St. Louis, MO: Mosby-Year Book; 1994:27–29.