

Quantitation of Renal Function

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This Continuing Education article is part of a series dealing with computerized quantitation of nuclear medicine studies. After reading and studying this paper the nuclear medicine technologist will be able to: 1) discuss the various methods used for differential functional analysis of the kidneys, and 2) compare methods for calculating effective renal plasma flow (ERPF) and glomerular filtration rate (GFR).

Quantitation of renal function has been performed for many years. Various methods have been developed and the introduction of computers to nuclear medicine has resulted in nuclear medicine studies of the kidney becoming a very powerful diagnostic tool. In this paper two approaches to computerized renal nuclear medicine are presented. The first approach deals with tubular function kinetics based on renal handling of orthoiodohippurate. The second approach is concerned with glomerular filtration kinetics (1). Comparison of various methods will show that the use of computers simplifies these procedures because the computer can handle these computations and the associated large amount of data with great speed.

QUANTITATION OF TUBULAR FUNCTION

True renal plasma flow can presently be measured directly using invasive methods. The compound whose clearance most closely approximates total renal plasma flow is *p*-aminohippuric acid (PAH) (2). Chemical analysis of PAH in blood and urine samples is very cumbersome; therefore, other chemical forms of hippuric acid have been used. Sodium ortho-iodohippurate (OIH) is commonly used to measure "effective" renal plasma flow (ERPF). The term effective is used to emphasize the difference between the *p*-aminohippuric acid (PAH) clearance value and the true value of renal plasma flow. This difference is small in the normal kidney (2). Effective renal plasma flow measured with OIH labeled with radioiodine correlates very well with the PAH method as long as the content of free radioiodine in the labeled OIH is less than 1.5%. The presence of free radioiodine lowers the clearance value of OIH. Orthoiodohippurate labeled with ¹³¹I is cleared both by glomerular filtration (20%) and tubular secretion (80%). As a result of its clearance, OIH gives sharper accumulation peaks and more rapid clearance times, and emphasizes renal function differences more distinctly than do agents cleared by glomerular filtration alone (2).

The uptake by normal kidneys of injected OIH is rapid,

reaching a maximum within the first 5 min. In a normally hydrated patient, the radiohippurate clears nearly completely within 30 min after injection and accumulates in the bladder with only minimal background activity present. If the patient voids and the bladder is completely emptied at this time, approximately 70% of the injected dose will be recovered in the collected urine (2). Relative dehydration delays both peak uptake and excretion.

Various methods have been developed to estimate ERPF. They can be categorized into two basic types: 1) camera imaging with data processing and 2) camera imaging with data processing and blood and urine collection. In this paper, we will describe an example of each type and give technical considerations for each. The method of choice for your department depends on available equipment and cost effectiveness, including time availability of the technologist (2).

Camera Images with Data Processing and Blood and Urine Collection

This method involves administration of 150 μCi ¹³¹I orthoiodohippurate per kidney (300 μCi total) with data collected over the kidneys at 1-min intervals for 27 min. One-minute images of the bladder are acquired before and after the patient voids. The injection site is also imaged to insure that the dose was not extravasated (Fig. 1). For calculation purposes, a 1:10,000 dilution of a duplicate dose is made. The detailed method for preparing this standard is published elsewhere (1).

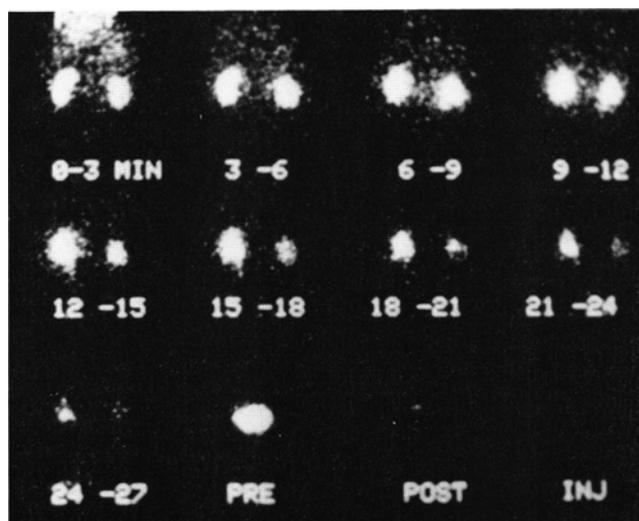


FIG. 1. Images (3 min/frame) from a comprehensive renal function study.

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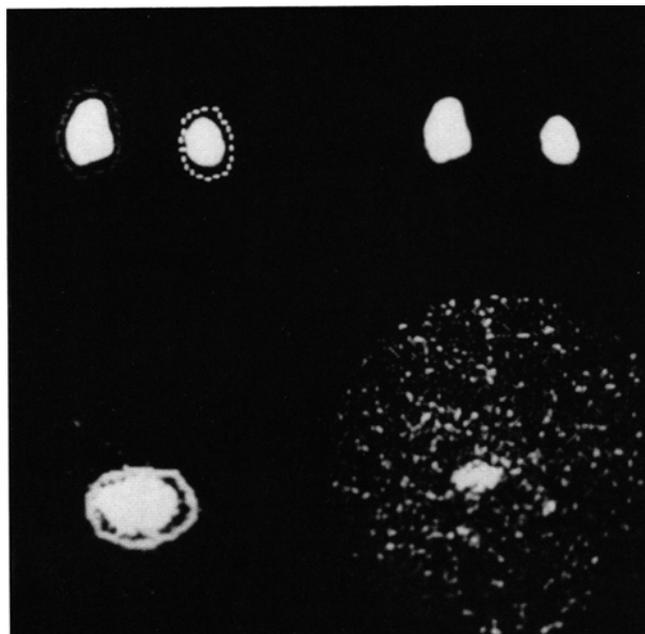


FIG. 2. Regions of interest for kidneys (upper left) and bladder images.

This method depends on a single blood sample collected at a specific time to represent the entire clearance curve. It was determined that 44 min is the optimal blood sampling time (2). The specific withdrawal time is important as specific coefficients for time intervals are required for the calculations. In addition to calculating the ERPF other useful indices are calculated, such as differential ERPF, actual percentage excretion, and excretory index. These indices require scintillation camera imaging, and in addition, excretion indices require a urine sample collected at 35 min.

The global ERPF at 44 min is calculated as follows:

$$\text{ERPF (ml/min)} = 1126.20 [1 - e^{-0.0080 (V_{44} - 7.80)}]$$

where V_{44} equals counts of the injected dose divided by counts in 1 liter of plasma at 44 min. Coefficients for other time periods can be found elsewhere (2). In order to calculate differential ERPF, computer processing of the kidney images is required. The differential ERPF is based on the right and left kidney uptake at 1 to 2 min. The formula used to calculate this is as follows:

$$\text{ERPF}_R = \text{ERPF} \times \frac{\text{Counts 1-2 min RK}}{\text{Counts 1-2 min RK} + \text{Counts 1-2 min LK}}$$

$$\text{ERPF}_L = \text{ERPF} - \text{ERPF}_R$$

where RK = right kidney and LK = left kidney. A composite image is obtained by adding the 27 images together and drawing a region of interest around each kidney (Fig. 2). The image should be normalized to the kidney pixels with the highest counting rate. The ROIs should be at least one pixel from the kidney edge. Counts from each kidney and the backgrounds

are obtained for the 1-2 min data. For background subtraction purposes a one-pixel-wide background region should be drawn around the left kidney. This kidney is chosen because the liver may elevate the background around the right kidney. Once the ROI selection is complete, net time-activity curves are generated for both kidneys (Fig. 3) and the background. The peak time for both kidney curves is stored for subsequent printout.

Next, the ROIs for the pre- and post-void bladder images are defined (Fig. 2). For background subtraction a one-pixel-wide ROI is generated around the bladder and net counts in the pre- and postvoid images are determined and stored (I).

Several calculations are made from the bladder image data and the urine specimen data. Expected excretion of the ^{131}I OIH at 35 min post-dose can be calculated as follows:

$$\text{Predicted dose (\%)} = 79.3 [1 - e^{-(0.004798 \times \text{ERPF})}]$$

The percentage of injected dose in the voided urine is calculated from the volume of urine excreted, the urine aliquot, and the activity in the dose itself.

Actual percentage of dose excreted at 35 min =

$$\frac{\text{Urine (counts/min)} \times \text{Urine volume} \times 100 (\text{dilution}) \times 100}{\text{Standard counts} \times 1000 (\text{dilution})}$$

The percentage dose retained and the residual urine in the bladder after voiding are calculated as follows:

Residual urine volume (ml) =

$$\frac{\text{Voided urine volume (ml)} \times \text{Postvoid net bladder counts/min}}{\text{Prevoid net bladder counts/min} - \text{Postvoid net bladder counts/min}}$$

Percentage dose in residual urine =

$$\frac{\text{Actual dose (\%)} \times \text{Residual volume (ml)}}{\text{Volume of voided urine (ml)}}$$

Total % dose = Actual % excreted + % Dose in residual urine

$$\text{Excretory index (EI)} = \frac{\text{Total \% excreted}}{\text{Predicted \% excreted}}$$

In this program, the excretory index (EI) is a built-in quality control checkpoint and should never exceed the value of 1.10 (I). A value higher than 1.1 indicates an error at some point, either in the ERPF estimation or in the total excretion calculation. A summary of all the calculations is printed for review by the physician (Fig. 4).

Advantages and Disadvantages

Certain technical considerations should be taken into account in order to assure accurate measurement of the ERPF. Quality control of the ^{131}I OIH is important. For accurate results, the ^{131}I OIH used should not contain more than 1.5% free iodide. Any extravasation of the dose invalidates the study. Improper dilution of the standard or samples can cause technical errors (I). Inattention to the plasma sampling time can

also cause improper estimates. Care should be taken when drawing ROIs because too-closely drawn ROIs can result in an incorrect calculation of the differential function.

Quantitation of renal function using the comprehensive renal function study can give an accurate estimate of the whole urinary tract. The introduction of computers has made quantitation of renal function even more convenient and accurate. This method has proven valuable to the clinician in monitoring patients with a single kidney or a graft, and those with acute and chronic renal failure, obstruction, and other renal pathology. It is easy to perform, but does require both computer processing and in vitro lab processing.

Effective Renal Plasma Flow Estimation Using A Gamma Camera Only

Effective renal plasma flow can be estimated from scintillation camera images and computer processing. Schlegel (2) studied the relationship between PAH clearance and the urinary excretion of radiohippurate at 30 min (predicted return) after a single intravenous dose. Predicted return according to Schlegel et al. (3) refers to the calculated return of radionuclide from the bladder based upon the uptake of the radionuclide by the kidneys. The correlation after correcting for residual urine in the bladder was found to be good. Further improvement in the correlation was made once the predicted return was corrected for body surface area. This made it possible to estimate the ERPF directly from the return (2).

The procedure involves calibrating the dose by counting it in a fixed position over the camera prior to injection. The patient is imaged for 10 min and the counts over the kidneys

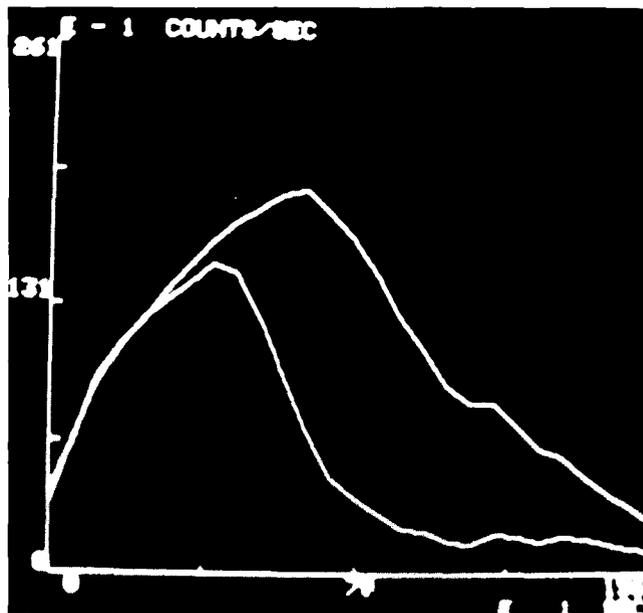


FIG. 3. Time-activity curves from a two-kidney patient.

in the 1-2 min post-injection period are used to measure the relative blood flow. This measure correlates with the 30-min predicted return (3). Therefore, the ERPF for each kidney can be estimated from the 1 to 2 min counts alone without counting urine or plasma. It should be noted that background and attenuation corrections are employed. The patient's height and weight are used to estimate tissue attenuation. Through further

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*****BIRMINGHAM V.A. MEDICAL CENTER*****
 *****RENOGRAPHIC DATA*****

NAME PATIENT ONE
 SOCIAL SECURITY NO. 000-00-0000
 AGE 63 SEX F BLOOD PRESSURE 120 / 60
 HEIGHT (IN) 66 WEIGHT (LBS) 168
 SURFACE AREA (M2) 1.86
 OIH DOSE 300 μ Ci ROI AREA LT 580 [58.0%] RT 420 [42.0%]

LEFT KIDNEY			RIGHT KIDNEY		
MIN	NT CT	%	MIN	NT CT	%
0-1	471	48.8	0-1	494	51.2
1-2	757	48.3	1-2	809	51.7
2-3	1004	48.7	2-3	1060	51.3
3-4	1192	48.7	3-4	1260	51.3
4-5	1420	49.8	4-5	1431	50.2
10-11	2134	69.9	10-11	920	30.1
15-16	1404	83.8	15-16	271	16.2
25-26	308	74.0	25-26	109	26.0

PEAK TIME LEFT: 11.0 MIN
 PEAK TIME RIGHT: 7.0 MIN

TOTAL ERPF AT 44 MIN
 IN ML/MIN = 412.5
 RIGHT: 213.1 LEFT: 199.4

URINE
 SPECIFIC GRAVITY: 1.005
 URINE VOL. (ML): 320.0
 EXPECTED EXCRETION: 68.3%
 ACTUAL VOID: 49.4%
 RESIDUAL URINE (ML): 17.2

TOTAL EXCRETION: 52.0%
 EXCRETORY INDEX: 0.76

FIG. 4. Example of the comprehensive renal function study report.

modification of this method, glomerular filtration rate and filtration fraction can be calculated (2).

This procedure, probably one of the most commonly used, is reported to be simple and economical because it does not require collection of a blood or urine sample and the imaging is completed in 10 min. The study is reported to be reproducible in an individual patient and therefore clinically applicable (2).

QUANTITATION OF GLOMERULAR FUNCTION

The glomerular filtration rate (GFR) is defined as the volume of plasma ultrafiltrate produced in 1 min in the renal glomeruli (2). The normal GFR is approximately 125 ml/min. The ratio between GFR and ERPF is called the filtration fraction (FF), and is usually 0.20 in normal patients (1).

Clearance of inulin, a mixture of fructose polymers with an average molecular weight of 5200, is traditionally accepted as the "gold standard" for measuring GFR. However, this is a rather tedious and time-consuming process, hence substances more easily measured would be beneficial.

Endogenous creatinine clearance, which involves an accurate 24-hr urine collection, was once hailed as the most popular method for rough estimation of GFR. Disadvantages of this test are the length of time involved and problems encountered in obtaining a complete (accurate) 24-hr urine collection. Creatinine clearance also is not an accurate measurement of GFR in diseased kidneys, since creatinine is excreted by the tubules as well as the glomeruli. It is possible to measure individual (differential) renal function with creatinine clearance, but this requires ureteral catheterization to collect urine from each kidney.

This is where nuclear medicine procedures can offer a simple, accurate, and reproducible GFR measurement that does not require urine collection. The length of patient test time varies from less than 10 min to 4–5 hr, depending upon the method selected. Global or differential measurements without invasive procedures are also an advantage.

Certain stringent requirements must be met before a radiopharmaceutical is considered ideal for GFR measurement. It must be freely filtered by the glomerulus and should not be retained in the kidney. It should not be bound (reversibly or irreversibly) to plasma proteins or other components in the blood nor reabsorbed (actively or passively) or secreted by the renal tubular epithelium. The radiopharmaceutical should be pure and chemically stable, as well as inert both metabolically and pharmacologically. Other ideal features include low radiation exposure to the patient and utilization of counting equipment readily available.

Radiopharmaceuticals

Various radiopharmaceuticals can be used, and the ideal choice will depend to some extent on whether a camera or blood clearance method is chosen. If techniques are employed in which values are obtained from blood clearance methods without urine collection or other means of external detection, the radiopharmaceutical must be cleared from circulation only by the kidneys and not by other organs and must not be bound by plasma proteins.

For values obtained by employing blood clearance methods, many consider ^{51}Cr -EDTA to be best. It is cleared from the circulation only by the kidneys with a global clearance corresponding closely to that of inulin. Unfortunately, this radiopharmaceutical is not commercially available in the U.S. For a comprehensive discussion of this agent, the reader is referred to the work of Bianchi (4).

A number of other chelated radioactive tracers have been found to correlate well with the results obtained with inulin. Included among these are $^{113\text{m}}\text{In}$ -DTPA, ^{111}In -DTPA, ^{169}Yb -DTPA, and ^{140}La -DTPA (2). Several agents stem from research on replacing stable iodine in radiographic contrast agents with ^{131}I or ^{125}I . Iodine-131-diatrizoate clearance has been found to correlate well with inulin in both adults and children and in pathologic and normal conditions (2). The same was found to be true of ^{131}I -iothalamate, currently the only radiopharmaceutical approved for routine GFR measurement in the U.S. Unfortunately, ^{125}I -iothalamate is not suitable for imaging.

Technetium-99m-DTPA has been used as a kidney imaging agent since 1970 (2). Its usefulness as a GFR agent was tested by comparing its clearance to that of inulin, iothalamate, and ^{51}Cr -EDTA. Although generally good correlation was demonstrated (5–11), it was found that accuracy of the results depended on the source of the commercial preparation (12). This was found to be most probably due to variation in the extent of plasma protein binding in the different manufacturers' products (2). The protein-bound portion that remains in circulation while the unbound activity is excreted can lead to significant error in GFR calculation. This problem can be solved in two ways. The first is to correct for protein binding in each patient by using a protein-free ultrafiltrate of the plasma and not whole plasma to calculate GFR. The second possible solution is not to use $^{99\text{m}}\text{Tc}$ -DTPA containing more than 1% protein-bound fraction, as assayed by quality control. The second option is recommended only in the clinical, and not the investigational, environment. Technetium-99m-DTPA is well-suited for camera methods because of its nearly ideal physical properties for imaging and its low radiation dose. It also allows combining of imaging with blood clearance methods to achieve differential as well as global function.

Camera Methods

Glomerular filtration rate measurements in nuclear medicine fall into one of two general categories. The first category employs a scintillation camera interfaced to a computer and is usually referred to as the camera method. The second category involves one or more blood samples and possibly the use of the camera, and is referred to as the blood clearance method. In the latter, a computer and camera are used only if differential measurement or images are desired.

Discussions about choice of method usually revolve around the respective accuracy of each method. One must also make sure, however, that the method chosen is appropriate for the equipment and personnel available and the environment in which the test is offered, i.e., for clinical or investigational purposes.

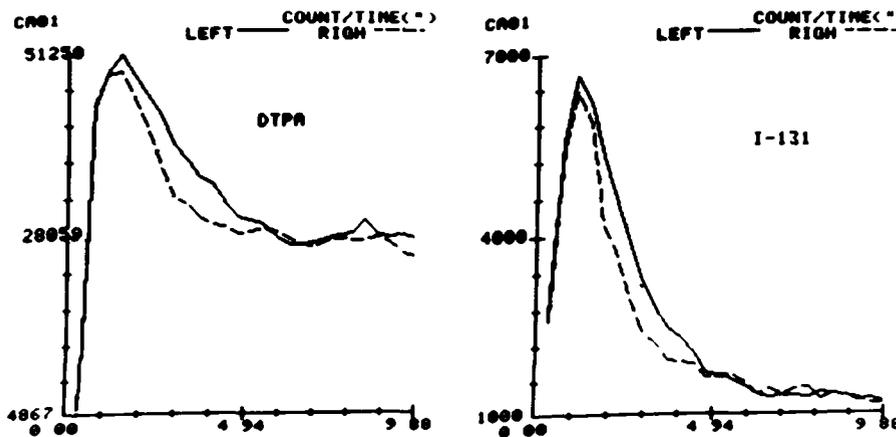


FIG. 5. Curves obtained from dual isotope study with ^{131}I -hippuran and $^{99\text{m}}\text{Tc}$ -DTPA. Comparison of hippuran and DTPA is shown to appreciate the different clearance rates of tubular versus glomerular agents.

Camera methods are simple, usually requiring less than 10 min of patient time. These methods can generate differential function and require only a scintillation camera interfaced to a computer. These methods certainly offer several distinct advantages over creatinine clearance, including drastically reducing the length of actual patient involvement as well as resolving problems associated with complete 24-hr urine collection and the rendering of differential function without invasive procedures, i.e., ureteral catheterization.

Camera methods are based on the fact that, after injection of an appropriate radiopharmaceutical, the differential GFR can be calculated from the net counts accumulated by each kidney during the first few minutes after injection. If the accumulated counts in the kidney are plotted versus time, a renal time-activity curve is obtained (Fig. 5). Careful examination of the curve reveals the arrival time of the bolus of activity in the kidney, the uptake of radiopharmaceutical by the kidney, and the peak time and rate at which the radiopharmaceutical is cleared from the kidney. Glomerular filtration rate is directly proportional to the accumulated counts during the uptake phase at which time the glomerular filtrate (or radiopharmaceutical) is in transit through the nephron and has not yet left the kidney (2). When attempting to calculate absolute GFR values by this method, however, several factors must be considered. One factor is tissue attenuation, which is dependent on the kidney depth and the energy of emissions of the isotope used. An estimate of attenuation correction can be obtained from renal depth, which can be measured by ultrasound or lateral scintigraphy, or estimated from the height and weight of the patient (3). Another factor to consider is the background activity, including that in the renal blood, renal extracellular space, and surrounding tissues (2). Various regions-of-interest (ROIs) have been proposed to correct for background activity, some with and some without interpolation (Fig. 6) (2). Some camera methods have been used without background correction (13,14) because the slope of the renal time-activity curve may be less sensitive to background correction.

One of the more widely used camera methods was introduced by Gates (15-17) in which the method for measurement of ERPF used previously by Schlegel was modified, corrected, and used to estimate GFR from renal accumulation of $^{99\text{m}}\text{Tc}$ -

DTPA (2). Simply stated, Gates recommends administering a carefully monitored dose of $^{99\text{m}}\text{Tc}$ -DTPA with pre- and post-injection counting of the syringe over the camera used for the study. Data acquisition begins at the time of injection. A large field-of-view camera with a parallel hole medium energy collimator interfaced to a digital computer is used. Special attention is given to the exact arrival time of the bolus in the renal ROI and to the kidney position. The best correlation derived from regression analysis with the traditional method of creatinine clearance was found by using the 2- to 3-min uptake corrected for depth and utilization of semilunar background ROI (Fig. 6E). Several factors must be considered to assure good results with this method. Stringent quality control of the camera and linearity of the dose response are of great value. One must also carefully evaluate the efficiency of data transmission from camera to computer, since count loss will invalidate the relationship between creatinine clearance and renal uptake.

Another popular camera method, which is used in Europe, is described by Piepsz et al. (18-19) and was tested mainly in

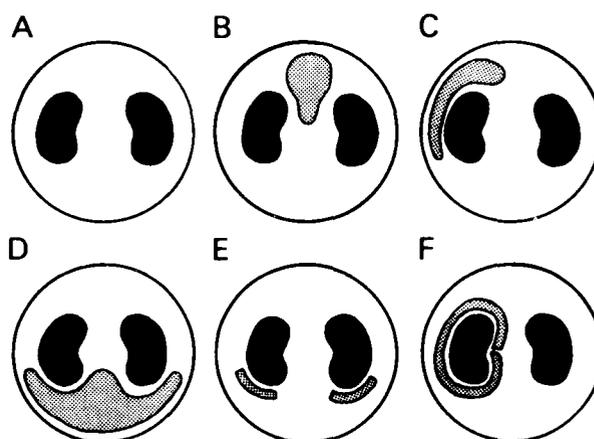


FIG. 6. Various ROIs used for background subtraction: (A) no correction; (B) ROI between kidneys; (C) ROI beside left kidney; (D) and (E) ROI below the kidneys; (F) ROI around left kidney. (Reprinted with permission from Grune & Stratton, Inc., @ 1982, Semin Nucl Med 12:308-329 and courtesy of E.V. Dubovsky and C.D. Russell.)

children. In addition to imaging, this method involves a single plasma sample drawn at 20 min after injection. Glomerular filtration rate is calculated by dividing the slope of the background-corrected renal curves (separate curves for each kidney) by the plasma concentration between 100 and 180 sec. The 20-min plasma sample and a precordial curve are used to determine the plasma concentration. This assumes that no significant amount of ^{99m}Tc -DTPA leaves the kidney during the first 3 min after injection and that the plasma curve is identical to the precordial curve. Good correlation was found between this method and results obtained using ^{51}Cr -EDTA.

Shore et al. (20) use a method of GFR determination in children that is based on an empirical correlation between ERPF and GFR, which are simultaneously evaluated with plasma disappearance of ^{99m}Tc -DTPA by single exponential analysis. They maintain that the tracer extraction rate of the kidney and plasma concentration must both be taken into account when expressing clearance. The rate of tracer uptake is measured by the renogram slope during the accumulation phase. Glomerular filtration rate (normalized for body surface area) is then correlated with a "normalized slope index," where slope index is defined as slope/A, in which $A = (\text{dose} \times \text{Std. counts})/(\text{Std.} \times \text{weight})$. While their accuracy appears comparable to that of other techniques, these investigators state the true value of this technique lies in its ability to provide maximum information from commonly performed imaging studies.

Rehling et al. (21,22) propose a method of calculating a single kidney glomerular filtration rate (SKGFR) in adults, as part of a ^{99m}Tc -DTPA renogram without determining the injected dose or collecting blood or urine samples. Since exact determination of the injected dose is not necessary, accidental (partial) extravasation of the dose would not invalidate this test.

Several sources of error exist for camera methods in general and usually occur in background correction, decay statistics, attenuation correction, estimation of arterial plasma activity, and system dead time (1). Most of these areas are included in the discussion of some of the various methods; however, we would like to comment briefly on the area of decay statistics. Due to the random nature of radioactive decay, substantial error can be introduced into camera methods that are based on renal time-activity curves. In fact, most of the observed error in some of these methods results from counting statistics (1).

Russell et al. (23) published a recent study comparing various methods [Piepsz et al. (18), Nielsen et al. (14), Assailly et al. (24), and Gates et al. (15-17)] with an independent GFR measurement based on an 8-point plasma clearance of ^{169}Yb -DTPA. This study concludes that scintillation camera methods can be substituted in clinical use for creatinine clearance and cites the added features of the camera method, i.e., no urine collection and ease of differential calculations. The authors state that the error of these methods (camera only with no blood samples) is approximately 20 ml/min, which is comparable to that reported for creatinine clearance.

Blood Clearance Methods

Blood clearance methods are based on the fact that GFR can be calculated from the rate of tracer activity clearance

from plasma following intravenous injection of an appropriate radiopharmaceutical by dividing the activity administered by the integral of the plasma time-activity curve. The requirements of an appropriate radiopharmaceutical have been discussed previously.

Although blood clearance methods do yield more accurate results, the short study time of camera methods is sacrificed. In blood clearance methods, multiple blood samples are collected over a period of 3 to 4 hr. An advantage of blood clearance methods is that radiotracers of ideal imaging properties are not required, since imaging is only an option. Chromium-51-EDTA is still used extensively in Europe, but, as previously stated, is not available commercially in the US. Dubovsky and Russell (2), in a review of renal quantification, state that ^{51}Cr -EDTA could be used to calculate GFR "from multiple plasma and urine samples, from a biexponential plasma disappearance curve, or from a single exponential fitted to the slow component of the curve."

Constable et al. (25), in adults, used an empirical correlation between ^{51}Cr -EDTA clearance measured from a 4-point curve and the ratio of injected activity in the plasma at 3 hr. They reported an error of 4.4 ml/min, using this ratio.

We would like to concentrate more, however, on a radiopharmaceutical that is available in the US and, in recent years, has been the focus of extensive testing—namely, ^{99m}Tc -DTPA. Technetium-99m-DTPA can be used to measure global GFR by constructing a disappearance curve from multiple blood samples, two samples (using a single exponential fitted through the points corresponding to the two samples), or a single sample drawn at a fixed time following injection (2).

The recently published method of choice in our laboratory (26), utilizes ^{99m}Tc -DTPA (dosage varies depending upon whether images are obtained). The single sample drawn 180 min after injection has only an 8 ml/min error, while the two-sample (60 and 180 min) method yields an error of only 4 ml/min. Technetium-99m-DTPA is administered in an intravenous injection taking care not to extravasate even a minute amount, as this will invalidate the results. This may be checked by either imaging or counting of the injection site. The syringe is flushed several times with blood, and correction is made for any residual activity greater than 3% of the injected dose. Sample(s) are drawn at the desired time from a different vein (opposite arm, if possible) than that used for injection. After centrifugation utilizing the Centrifree apparatus*, a protein-free ultrafiltrate of the plasma is obtained. The ultrafiltrate is then counted along with a standard obtained by dilution of a dose identical to that used for injection.

In calculation of GFR by single sample at 180 min (26):

$$\text{GFR (ml/min)} = A \ln (D/P) + B$$

where $D =$ administered activity (in counts/min)

$P =$ plasma activity (in counts/min/ml)

$T =$ time between injection and drawing of sample (in min)

$A = -0.278T + 119.1 + 2405/T$

$B = 2.886 - 1222.9 - 16,820/T$

$\text{GFR (ml/min)} = 82.42 \ln (D/P) - 800.5$

In calculation of GFR with two samples (60 and 180 min) for improved accuracy (25):

$$\text{GFR} = \left[\frac{D \ln (P_1/P_2)}{T_2 - T_1} \exp \left(\frac{(T_1 \ln P_2) - (T_2 \ln P_1)}{T_2 - T_1} \right) \right]^{0.979}$$

where D = dose activity (counts/min)

P₁ = plasma activity at T₁ × 0.94

P₂ = plasma activity at T₂ × 0.94

P₁ and P₂ are in counts/min-ml

For additional review, beyond the scope of this paper, of all aspects of blood sampling methods for GFR measurement, the reader is referred to a recently published article by Brochner-Mortensen (27).

In summary, while blood clearance methods do yield more accurate results, these require additional counting equipment, i.e., a scintillation counter, technological skills, and related equipment for handling in vitro specimens. It is stressed that, no matter which method is chosen, inappropriate equipment, suboptimal technique, or unskilled personnel will yield unreliable results and discredit the test.

NOTE

*Amicon Centrifree Micropartition System (MPS-1), Amicon Corporation, Danvers, MA.

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REFERENCES

1. Dubovsky EV, Gates GF, Russell CD. Three approaches to computer-assisted function studies of the kidney and evaluation of scintigraphic methods. In: Tauxe WN, Dubovsky EV, eds. *Nuclear Medicine in Clinical Urology and Nephrology*. Norwalk, Connecticut: Appleton-Century-Crofts, 1985:157-189.
2. Dubovsky EV, Russell CD. Quantitation of renal function with glomerular and tubular agents. *Semin Nucl Med* 1982;12:308-329.
3. Thompson IM Jr, Boineau FG, Evans BB, et al. The renal quantitative scintillation camera study for determination of renal function. *J Urol* 1983;129:461-465.
4. Bianchi C. Measurement of the glomerular filtration rate. *Prog Nucl Med* 1972;2:21-53.
5. Klopfer JF, Hauser W, Atkins HL, et al. Evaluation of ^{99m}Tc-DTPA for the measurement of glomerular filtration rate. *J Nucl Med* 1972;13:107-110.
6. Barbour GL, Crumb CK, Boyd CM, et al. Comparison of inulin, iohalamate and ^{99m}Tc-DTPA for measurement of glomerular filtration rate.

J Nucl Med 1976;17:317-320.

7. Brochner-Mortensen J. Routine methods and their reliability for assessment of glomerular filtration rate in adults. *Dan Med Bull* 1978;25:181-202.
8. Hilson AJW, Mistry RD, Maisey MN. ^{99m}Tc-DTPA for the measurement of glomerular filtration rate. *Br J Radiol* 1976;49:794-796.
9. Rossing N, Bojsen J, Fredriksen PL. The glomerular filtration rate determined with ^{99m}Tc-DTPA and a portable cadmium telluride detector. *Scand J Clin Lab Invest* 1978;38:23-28.
10. Rootwelt K, Falch D, Sjøkvist R. Determination of glomerular filtration rate (GFR) by analysis of capillary blood after single shot injection of ^{99m}Tc-DTPA. A comparison with simultaneous ¹²⁵I-iothalamate GFR estimation showing equal GFR but difference in distribution volumes. *Eur J Nucl Med* 1980;5:97-102.
11. Agha N, Persson RBR. Comparative labelling and biokinetic studies of ^{99m}Tc-EDTA (Sn) and ^{99m}Tc-DTPA (Sn). *Nuklearmedizin* 1977;16:30-35.
12. Russell CD, Rowell K, Scott JW. Quality control of Technetium-99m-DTPA: Correlation of analytic tests with in vivo protein binding in man. *J Nucl Med* 1986;27:560-562.
13. Tamminen TE, Riihimäki EJ, Tahti EE. A gamma camera method for quantitation of split renal function in children followed for vesicoureteric reflux. *Pediatr Radiol* 1978;7:78-84.
14. Nielsen SP, Lehd-Møller M, Trap-Jensen J. ^{99m}Tc-DTPA scintillation camera renography: A new method for estimation of single kidney function. *J Nucl Med* 1977;18:112-117.
15. Gates GF. Glomerular filtration rate: Estimation from fractional renal accumulation of ^{99m}Tc-DTPA (stannous). *Am J Roentgenol* 1982;138:565-570.
16. Gates GF. Split renal function testing using Tc-99m-DTPA: A rapid technique for determining differential glomerular filtration. *Clin Nucl Med* 1983;8:400-407.
17. Gates GF. Computation of glomerular filtration rate with Tc-99m-DTPA. An in-house computer program. *J Nucl Med* 1984;25:613-618.
18. Piepsz A, Dobbeleir A, Erbsmann F. Measurement of separate kidney clearance by means of ^{99m}Tc-DTPA complex and a scintillation camera. *Eur J Nucl Med* 1977;2:173-177.
19. Piepsz A, Denis R, Ham HR, et al. A simple method for measuring separate glomerular filtration rate using a single injection of ^{99m}Tc-DTPA and the scintillation camera. *J Pediatr* 1978;93:769-774.
20. Shore RM, Koff SA, Hays JR, et al. Glomerular filtration rate in children: Validation and longitudinal use of determination from the Tc-99m-DTPA renogram. *Am J Kid Dis* 1986;8:170-180.
21. Rehling M, Møller ML, Lund JO, et al. ^{99m}Tc-DTPA gamma-camera renography: Normal values and rapid determination of single-kidney glomerular filtration rate. *Eur J Nucl Med* 1985;11:1-6.
22. Rehling M, Møller ML, Thamdrup B, et al. Reliability of a ^{99m}Tc-DTPA gamma camera technique for determination of single kidney glomerular filtration rate. *Scand J Urol Nephrol* 1986;20:57-62.
23. Russell CD, Bischoff PG, Kontzen F, et al. Measurement of glomerular filtration rate using ^{99m}Tc-DTPA and the gamma camera: A comparison of methods. *Eur J Nucl Med* 1985;10:519-521.
24. Assailly J, Pavel DG, Bader C. Noninvasive experimental determination of the individual kidney filtration fraction by means of a dual-tracer technique. *J Nucl Med* 1977;18:684-691.
25. Constable AR, Hussein MM, Albrecht MP, et al. Renal clearance determination from single plasma sample. In: Hollenberg N, Lange S, eds. *Radionuclides in Nephrology*. New York: Thieme-Stratton, 1980:62-66.
26. 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.
27. Brochner-Mortensen J. Current status on assessment and measurement of glomerular filtration rate. *Clin Physiol* 1985;5:1-17.