GFR Determination by a Modification of the Gates Method: The Conventional Renal Examination with a Semi-Automated GFR Measurement

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The conventional radionuclide renal examination using a 10–20-mCi dose of technetium-99m (^{99m}Tc) DTPA (Pentetate), conducted over a 30–60-min duration, does not accommodate the Gates method for GFR determination. Simple modifications to the Gates technique will, however, permit a GFR determination to be made without sacrificing the components of a complete conventional renal examination, and will not significantly alter the technologist's examination routine or time commitment. These modifications allow the Gates method to be used on virtually any gamma camera/collimator combination with an accompanying computer system, dose calibrator, and a lead slab syringe attenuator. With the modifications, GFR determinations can be obtained using doses of tracer as high as 10–20 mCi, while eliminating the direct gamma camera counting of the residual activity in the post-injection syringe. The net injected syringe counts are calculated using the gamma camera counts from the preinjection syringe attenuated through lead and the dose calibrator's pre- and postinjection measurements of activity to determine the fraction of injected counts from the measured syringe dose. Excellent results are obtained when the gamma camera counts of the syringe activity using the original Gates method are compared to the counts derived from the modified technique using the lead slab attenuator and the dose calibrator ($r > 0.99$). We have found that this particular modification of the Gates method allows for a full examination by removing the dose and time restrictions imposed by the original Gates technique.

The purpose of this manuscript is not to prove or disprove the validity of the Gates glomerular filtration rate (GFR) method (*1*), but rather is to demonstrate the validity of modifying the Gates method for those that use this technique to provide a quantitative relative measurement of renal function (*2*). The Gates method of GFR determination has been shown to have precision (reproducibility) with a linear correlation factor of $r > 0.99$ between paired studies of 15 kidneys measured and repeated 24 hr apart (*3*). The accuracy of the GFR value has been shown to be deficient. Reportedly, depth correction by the Tonnesen equations has been identified as a major factor in reducing the Gates method accuracy (*4*).

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The technetium-99m (^{99m}Tc) DTPA (Pentetate) renal examination (*5,6*), using a gamma camera with computer acquisition and analysis programs to determine the total and individual kidney GFR, as described by Gates (*3,7,8*), is modified to allow for injections of as much as 10–20 mCi of ^{99m}Tc-DTPA. The Gates method for the determination of GFR routinely uses a ^{99m}Tc-DTPA dose of 3.0 mCi or less, with the syringe placed 30 cm from the face of the collimator to avoid camera deadtime counting losses and computer pixel overflow. The syringe is counted before and after injection. With our modification of this technique, a syringe with 10–20 mCi of ^{99m}Tc-DTPA is counted at 30 cm from the face of the collimator through a 2-mm lead attenuator (111 × attenuation). The activity measured in the syringe by the dose calibrator, before and after injection, is used to calculate the fraction of activity that was injected into the patient. The injected fraction of tracer and the lead attenuation factor are applied to the lead attenuated preinjection syringe gamma camera counts to calculate the net injected counts per one minute. With these modifications applied to the Gates technique, doses of 10–20 mCi of ^{99m}Tc-DTPA can be used to give us sufficient imaging data for a complete renal scan with computer analysis, including a determination of GFR.

MATERIALS AND METHODS

Calibration

A Siemens Orbiter gamma camera* fitted with its low-energy all-purpose collimator connected to a Medical Data Systems A^2 computer system†** running M.I.P.S. version 1.0 software provided the imaging and computer functions. The pulse-height analyzer peak was set to match the photopeak of ^{99m}Tc with a 15% window. Two large styrofoam cups glued together at their bottoms were used to elevate and support the lead shield attenuator to 30 cm above the collimator surface (Fig. 1). Gamma camera counts obtained from lead shield attenuated syringes were analyzed using linear regression against the Capintec CRC-5 dose calibrator† millicurie measurements. Nine syringes containing ^{99m}Tc-DTPA doses of 23.50, 16.99, 12.80, 7.80, 4.43, 3.03, 1.37, 0.35, and 0.18 mCi were measured. A calibrated lead syringe shield attenuator (111 × attenuation) allows the gamma camera and

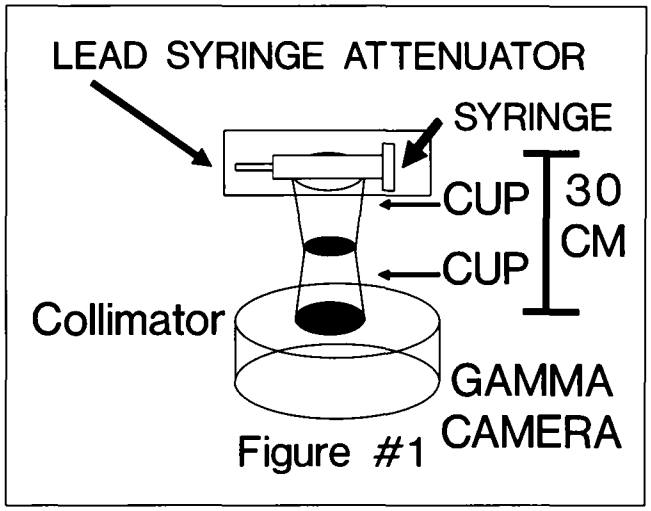

FIG. 1. Two large styrofoam cups glued together at their bottoms are used to elevate and support the lead shield attenuator to 30 cm above the collimator surface.

computer combination to record counts in the linear range of the system. The activity from each syringe is acquired as a 1-min 64 × 64 pixel word (16 bit) mode static image. Region measurements of the static images are used to obtain the counts from the lead attenuated syringes. Isocount regions of interest set to include 1%–100% of the counts within the outlined region are used for count measurements. These counts are then plotted against the mCi dose values of the syringes. Linear regression analysis is performed to determine the linearity of the system. The measured lead attenuated counts are corrected by the lead attenuation factor (111 × attenuation) to obtain the actual counts that are used in the Gates equation. Less than 5 min of time was needed to record the dose calibrator's measurement of syringe activity and record the syringe using the described method with the gamma camera. Decay correction was not performed since less than a 1% loss of activity occurs within 5 min.

CLINICAL APPLICATION

Prior to the ^{99m}Tc-DTPA renal study, the patient's age, sex, height, weight, and serum creatinine (if available) were recorded. For the average 70-kg patient, a dose of 15 mCi of ^{99m}Tc-DTPA was drawn. The syringe was placed into the dose calibrator, measured using the 20-mCi range setting, and the dose was then recorded. When measuring the amount of activity in the syringes, attention was directed to place the preinjection syringe and the postinjection syringe into the dose calibrator at the same position in an effort to insure precise measurements of activity obtained with similar dose calibrator geometry.

The ^{99m}Tc-DTPA syringe dose was centrally positioned on a 2-mm lead syringe attenuator (111 × attenuation) and placed 30 cm from the face of the low-energy collimator of the gamma camera by using the two glued styrofoam cups. A 1-min static image was acquired by the computer.

After the patient was injected with the ^{99m}Tc-DTPA dose, the syringe was placed into the dose calibrator in the same position where the preinjection syringe was placed. The remaining activity was read on the 20-mCi range setting and recorded.

A 1-min static image of the ^{99m}Tc-DTPA injection site was acquired on the computer to identify any infiltration of tracer, which can invalidate the GFR determination.

The renal study using ^{99m}Tc-DTPA was imaged on the gamma camera in two phases. The first phase was a renal blood flow (perfusion) scan with dynamic images acquired every 2 sec for nine images. The second phase was the renal (function) scan, which begins with a "750K immediate" analog image. Static analog images are then taken every 5 min for the 30- or 60-min study, adjusted for the time required to obtain the "750K immediate" image. The counts for each image are then recorded. Simultaneously, a two-phase computer acquisition begins at the time of injection, using 1 sec per frame for 60 frames (perfusion phase), and continues into phase two (function phase) at 30 sec per frame for 60 or 120 frames. For all computerized image acquisitions, a 64 × 64 word (16 bit) mode matrix without magnification was utilized.

A computer program for GFR determinations was created and uses the method reported by Gates (*1*), with the necessary modifications made to correct for the lead attenuation and the fraction of the dose that was administered for the study as determined by the dose calibrator measurements of activity. The software was written in Fortran IV, compiled, linked, and loaded via predefined sequences incorporated into the M.I.P.S. menu system allowing for semi-automated renal acquisition and analysis. The basic Gates equation (3) and region of interest assignments are preserved, except for the denominator of the equation where the net injected counts per one minute are calculated. The following equations demonstrate how the modification is incorporated in the Gates equation.

$$\text{Gates Method GFR} = \frac{[(\text{Rt. k cts} - \text{bkg})/e^{-\mu XR}] + [(\text{Lt. k cts} - \text{bkg})/e^{-\mu XL}]}{(\text{Preinjection cts} - \text{Postinjection cts})} \times 100\% \times 9.81270 - 6.82519 \quad \text{(Eq. 1)}$$

Kidney depth (measured in cm) is determined by the patients' height, ht, (measured in cm) and the patients' weight, wt, (measured in kg), where xR = right kidney and xL = left kidney.

$$xR = [(wt/ht) \times 3.3] + 0.7 \quad \text{(Eq. 2a)}$$

$$xL = [(wt/ht) \times 3.2] + 0.7 \quad \text{(Eq. 2b)}$$

$$\text{Modified Method GFR} = \frac{[(\text{Rt. k cts} - \text{bkg})/e^{-\mu XR}] + [(\text{Lt. k cts} - \text{bkg})e^{-\mu XL}]}{[(\text{Preinj. cts})(LF)] - [(\text{mCi post/mCi pre})(\text{preinj. cts})(LF)]} \times 100\% \times 9.81270 - 6.82519, \quad \text{(Eq. 3)}$$

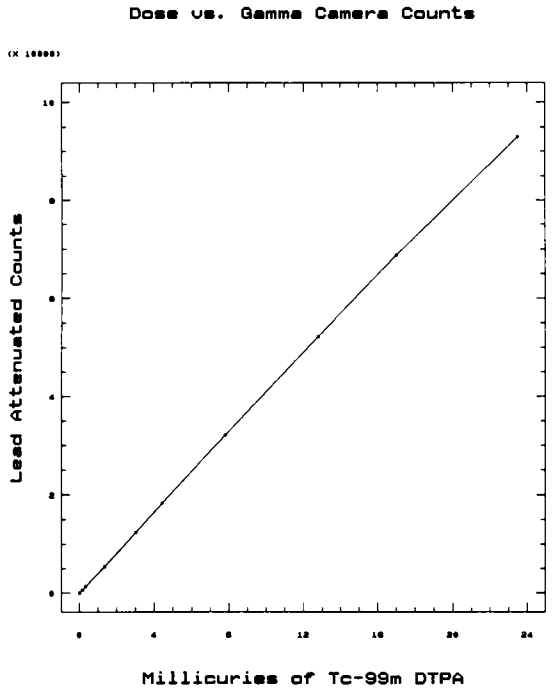

FIG. 2. Results obtained from plotting the lead attenuated counts against the mCi values demonstrate a straight line fit.

where LF, the lead attenuation factor, = 111.

Algebraically, this denominator becomes:

$$[(\text{preinj. cts})(\text{LF})] \times [(\text{mCi pre} - \text{mCi post})/\text{mCi pre}] = \text{the net counts injected into the body.} \quad \text{(Eq. 4)}$$

Thus,

Modified Method GFR =

$$\frac{[(\text{Rt. k cts} - \text{bkg})/(e^{-\mu XR}) + (\text{Lt. k cts} - \text{bkg})/(e^{-\mu XL})]}{[(\text{preinj. cts})(\text{LF})] \times [(\text{mCi pre} - \text{mCi post})/(\text{mCi pre})]} = 100\% \times 9.81270 - 6.82519] \quad \text{(Eq. 5)}$$

RESULTS

Prior to implementing the modification, syringes containing activity ranging from 0.18 - 23.5 mCi were measured through the lead attenuator using the described technique. Results obtained from plotting the lead attenuated counts against the mCi values demonstrate a straight line fit (Fig. 2). Linear regression of this fit yielded an $r > 0.9998$, indicating the linearity of the dose calibrator and the linearity of the gamma camera and computer system (Fig. 3). This high degree of linearity assures little, if any, camera deadtime or pixel overflow interfering with the syringe measurements. The lead attenuation factor is a well established value for ^{99m}Tc and was measured specifically for the approximately 2-mm thick syringe attenuator to be 111 × (i.e., activity is reduced by 1/111th of the original value as recorded through the lead at the energy range of ^{99m}Tc). The results of the linear regression fit support the derivation and use of Equation 18. (See Appendix for the derivation of Equation 18 and proof of linearity conservation.)

$$\text{LF} \times \text{gamma camera counts(A)} \times \left(\frac{\text{mCi's(A)} - \text{mCi's(B)}}{\text{mCi's(A)}}\right), \quad \text{(Eq. 18)}$$

where (A) denotes preinjection syringe dose, (B) denotes postinjection syringe dose, and LF denotes the lead attenuation factor (111 ×).

Equation 18 is dependent only on the gamma camera reading of the preinjection syringe and the dose calibrator's activity readings of the pre- and postinjection syringes. Thus, gamma camera counting of the postinjection syringe can be eliminated. Equation 5 is the end result of incorporating Equation 18 into Equation 1 by replacing the denominator of the original Gates equation with Equation 18.

A trial of 13 patients comparing the original Gates method to the modified Gates method gave a reasonable linear correlation with an $r > 0.953$ (Fig. 4). Syringe doses ranged from 0.06 = 3.06 mCi as to allow the original Gates method to be performed for the comparison. Doses greater than 5 mCi caused noticeable pixel overflow (i.e., near zero -

Regression Analysis - Linear model: Y = a+bX

Dependent variable: GFRSYR.HILEADCO Independent variable: GFRSYR.HIMCI

Parameter	Estimate	Standard Error	T Value	Prob. Level
Intercept	227.4	275.377	0.825776	.43287
Slope	3996.98	26.2989	151.983	.00000

Analysis of Variance

Source	Sum of Squares	Df	Mean Square	F-Ratio	Prob. Level
Model	9.5872E0009	1	9.5872E0009	2.310E0004	.00000
Error	3320427.5	8	415053.4		
Total (Corr.)	9.5905E0009	9			

Correlation Coefficient = 0.999827 R-squared = 99.97 percent
Stnd. Error of Est. = 644.246

FIG. 3. Linear regression yielded a correlation coefficient of $r > 0.9998$ between the dose calibrator and the gamma camera and computer system. This high degree of linearity assures little if any camera deadtime or pixel overflow interfering with the syringe measurements.

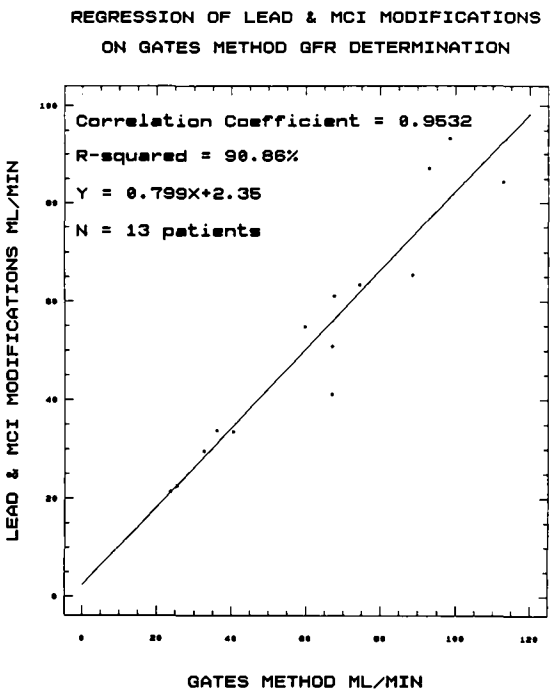

FIG. 4. Comparison of the original Gates method to the modified Gates method by linear regression in 13 patients.

valued pixels intermixed with high count pixels) on computer acquired images of the syringes and, thus, were not included for this comparison.

DISCUSSION

By using a 2-mm lead syringe attenuator, the 10.0–20.0-mCi dose of ^{99m}Tc-DTPA can be accurately counted without significant gamma camera deadtime losses or computer pixel overflow, as shown by the excellent linear correlation coefficient ($r > 0.9998$) between the millicurie dose readings and the digitized lead attenuated gamma camera counts. The 2 mm of lead provide ~7 half-value layers of attenuation for ^{99m}Tc, which reduces the observed activity at the 30 cm distance from the face of the collimator to 1/111th of the actual activity. The lead factor, LF, therefore, is equal to 111. The recorded gamma camera counts of the lead attenuated syringe dose is multiplied by the lead factor to obtain the unattenuated preinjection syringe counts. The dose calibrator readings of the preinjection and postinjection measurements of activity are linear, as required by the standard operating procedures for quality control of any nuclear medicine department. By calculating the measured millicurie fraction expelled from the syringe after injection, the net injected counts can be determined. The net injected counts are calculated from the initial gamma camera recording of the lead attenuated preinjection syringe dose multiplied by the lead factor and by the fraction of the syringe dose that was expelled from the syringe, assuming no extravasation or other loss of tracer has occurred. Incorporation of these modifications into the Gates equation results in a technique that allows for the simultaneous acquisition of a conventional 10.0–20.0-mCi ^{99m}Tc-DTPA renal scan with complete perfusion and functional images, and a GFR by the established Gates method.

APPENDIX

The following mathematical proof is presented in derivation of Equation 18 from Equation 6. Both the dose calibrator and gamma camera are known to be linear within bounded ranges of use. In the following derivation, linearity is maintained. Equation 6 relates millicuries of activity to gamma camera counts and is the basis for the derivation. It is assumed that attenuation by lead remains constant for the selected isotope and will be referred to as "lead factor" or "LF."

$$\text{mCi's} \times k = \text{lead factor} \times \text{gamma camera counts} \quad \text{(Eq. 6)}$$

or

$$\text{mCi's} \times k = \text{syringe counts}, \quad \text{(Eq. 7)}$$

where k is a proportionality constant and "lead factor × gamma camera counts" are the lead shield attenuation corrected gamma camera counts of a syringe.

Now (A) denotes preinjection and (B) denotes postinjection.

$$\text{mCi's(A)} \times k = \text{lead factor} \times \text{gamma camera counts(A)} \quad \text{(Eq. 8)}$$

$$\text{lead factor} \times \text{gamma camera counts(A)} = \text{syringe counts(A)} \quad \text{(Eq. 9)}$$

$$k = \frac{\text{lead factor} \times \text{gamma camera counts(A)}}{\text{mCi's(A)}} \quad \text{(Eq. 10).}$$

Likewise,

$$\text{mCi's(B)} \times k = \text{lead factor} \times \text{gamma camera counts(B)} \quad \text{(Eq. 11)}$$

$$\text{mCi's(B)} \times k = \text{syringe counts(B)} \quad \text{(Eq. 12)}$$

Net injected counts:

$$\text{preinjection syringe counts} - \text{postinjection syringe counts} \quad \text{(Eq. 13)}$$

or

$$\text{syringe counts(A)} - \text{syringe counts(B)} \quad \text{(Eq. 14)}$$

or substituting: Equation 9 for syringe counts (A) and Equation 12 for syringe counts (B), we obtain:

$$\text{lead factor} \times \text{gamma camera counts(A)} - \text{mCi's(B)} \times k \quad \text{(Eq. 15)}$$

Substituting for k using Equation 10 where lead factor = LF:

$$\text{LF} \times \text{gamma camera counts(A)} - \text{mCi's(B)}$$

$$\times \frac{\text{LF} \times \text{gamma camera counts(A)}}{\text{mCi's(A)}} \quad \text{(Eq. 16)}$$

Factoring out common terms:

$$\text{LF} \times \text{gamma camera counts(A)}$$

$$\times \left(1 - \frac{\text{mCi's(B)}}{\text{mCi's(A)}}\right) \quad \text{(Eq. 17)}$$

or

$$\text{LF} \times \text{gamma camera counts(A)}$$

$$\times \left(\frac{\text{mCi's(A)} - \text{mCi's(B)}}{\text{mCi's(A)}}\right) \quad \text{(Eq. 18)}$$

Incorporation of Equation 18 into Gates equation yields:

Equation 5 Modified Method GFR =

$$\frac{\dfrac{\text{Rt. k cts} - \text{bkg}}{e^{-\mu XR}} + \dfrac{\text{Lt. k cts} - \text{bkg}}{e^{-\mu XL}}}{(\text{Preinj. cts} \times \text{LF}) \times \left(\dfrac{\text{mCi pre} - \text{mCi post}}{\text{mCi pre}}\right)} \times 100\% \times 9.81270 - 6.82519.$$

NOTES

* Siemens Gammaonics, Schaumburg, IL.
† Medical Data Systems, Ann Arbor, MI
‡ Capintec, Inc., Ramsey, NJ.

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