Noninvasive Experimental Determination of the Individual Kidney Filtration Fraction by Means of a Dual-Tracer Technique

Jacques Assailly, Dan G. Pavel, Cyrille Bader, Jacques Chanard, Thomas W. Ryerson, Jean-Pierre Cotard, and Jean-Louis Funck-Brentano

Necker Hospital, University of Paris, Paris, France, and University of Illinois Hospital and Columbus Hospital, Chicago, Illinois

A noninvasive method for measurement of the individual kidney filtration fraction (FF) is presented, based on an analysis of the early rise of the kidneys' time–activity curves obtained after simultaneous injection of tubular [^{131}I] ortho-iodohippurate and glomerular (Tc-99m DTPA) tracers. The analysis is based on the assumption that an insignificant amount of tracer leaves the kidney during the first few moments following injection. Therefore the kidney activity during this period is directly proportional to the integral of the blood (heart) activity. The dual-tracer technique allows the direct calculation of the ratio of glomerular to tubular clearances, i.e., the FF. In vivo studies were performed on 12 dogs, including normals as well as others with acute ureteral ligation or Benemid-induced tubular blockade. The calculated FF correlated well with the FF obtained from single-shot clearances performed simultaneously. We conclude that the FF can be calculated directly for each kidney, noninvasively, from the early part of the tubular and glomerular time–activity curves by noninvasive external detection.

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The need for noninvasive methods using radionuclides for the evaluation of the kidney function has been stressed by clinicians. The renogram with [^{131}I] ortho-iodohippurate represents a typical noninvasive method; it can provide a certain amount of valuable information if properly performed and interpreted, but nevertheless it has definite limitations. The main limitation is that the renogram expresses a complex function resulting from the superimposition of multiple physical and physiologic factors including geometry, background, renal hemodynamics, and the various nephron mechanisms (*1*). For the interpretation of the renogram, two general approaches have been suggested: (A) the analysis of different segments of the curve (*2–4*)—an approach that has been disappointing overall—and (B) the evaluation of the curve as a whole with or without mathematical simulation (*5–7*). One of the most serious limitations of all these methods is that they do not solve the problem of the nonspecificity of the so-called cumulative type of curve, which is encountered in a variety of clinical situations such as ureteral obstruction and acute renal failure in the polyuric stage (*8*). The limitations of the methods using radionuclides to measure split renal function are of two types: (A) related to the simplifications or hypotheses used to approximate the model for kidney-tracer dynamics (*9*) or (B) related to the approximations concerning the external detection of the radioactivity from each kidney (*10,11*).

In previous studies (*12*) evaluating the function of

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For reprints contact: Jacques Assailly, INSERM Centre de Technologie Biomedicale, 149 Rue de Sevres, 75015 Paris, France.

isolated pig kidneys, we tried to circumvent this limitation by using two radionuclides: [^{131}I] ortho-iodohippurate (Hippuran®) and [^{125}I] sodium diätrizoate (filtered). Under these circumstances, the part of the time–activity curve obtained immediately after intra-arterial injection (i.e., before recirculation occurs) allowed the calculation of a plateau-to-peak ratio, which represents the fraction of the dose remaining in the kidney. This ratio is the extraction ratio for the tracer, derived from the arteriovenous difference. The ratio of the two extraction ratios for the glomerular and tubular curves has proven to be a sensitive index of renal function in isolated kidneys with varying degrees of tubular damage (*12*).

We have subsequently tried to extend this technique to kidneys in situ. In contradistinction to the isolated kidney circuit, it is necessary in this case to consider the renal response to an intravenous injection with recirculation of tracers. A true renal time–activity curve can be determined by appropriate correction for vascular background activity, geometry, and detector efficiency. The correction is made possible by the use of intravascular tracers and simultaneous recording of the precordial or subclavicular-count rates fossa (*1,13–15*). We have shown, by a mathematical analysis, that it is possible to determine noninvasively a glomerulo/tubular ratio (G/T ratio), i.e., the filtration fraction (FF) for each kidney, analyzing only the early rise of the true [^{131}I] Hippuran and Tc-99m DTPA renogram curves. We present here this analysis and its experimental verification in unilaterally nephrectomized but otherwise normal dogs.

THEORETICAL ANALYSIS

Using the mathematical approach described in the Appendix, we were able to obtain by external detection a quotient representing the ratio between the values of the Tc-99m DTPA and the [^{131}I] ortho-iodohippurate extraction ratios:

$$\frac{G}{T} = K\frac{\sigma_G}{\sigma_T}. \qquad (1)$$

This quotient represents the filtration fraction, and is proportional to the slopes obtained by processing the DTPA and Hippuran curves (renal and precordial) as described in the Appendix.

MATERIALS AND METHODS

Twelve anesthetized, unilaterally nephrectomized dogs were used. The nephrectomy was performed at least 3 weeks before the test. Two of the dogs were also given 25 mg/kg Benemid* intravenously (*16*). In four other dogs acute ureteral ligation was done surgically half an hour before the experiment.

Two NaI(Tl) probes with cylindrical collimation (diameter 4 cm, depth 7 cm), were connected to a four-track magnetic tape recorder. The data from the magnetic tape were played back into an 800-channel analyzer with a time constant of 5 sec; they were also stored in digital form on a punched paper tape and subsequently analyzed with a laboratory computer.

[^{131}I] ortho-iodohippurate, Tc-99m DTPA, and iodine-tagged human serum albumin (I-131 HSA) were used. A sample of the dog's red blood cells (RBC) was labeled in vitro with Tc-99m about 1 hr before the injection (*17*). The bladder was catheterized. One probe was placed over the heart and another over the kidney area. A continuous infusion of isotonic saline was given during the procedure, to ensure a urine output of approximately 2 ml/min. The following protocol was then used.

1. The background was recorded for 3 min on the four channels for kidney I-131, kidney Tc-99m, heart I-131, and heart Tc-99m respectively. The first blood sample was drawn for background level.
2. I-131 HSA (6 μCi) was injected for measurement of the vascular component. After a 5-min equilibration period, the radioactivity was recorded for 2 min on each of the four channels. A second blood sample was drawn at the end of this period.
3. Tc-99m RBC (20 μCi) was then injected. Five minutes later the resulting activity was recorded for 2 min on the four channels. A third blood sample was drawn.
4. A solution containing [^{131}I] ortho-iodohippurate (40 μCi) and Tc-99m DTPA (120 μCi) was finally injected and the corresponding activity was recorded on the four channels for 10 min.
5. Blood samples were drawn at 30, 40, 60, and 80 min after the last injection and were counted in a well counter set up for dual-nuclide counting. The clearances were calculated by the simplified single-shot method (*18,19*).

The remaining calculations were performed using a FORTRAN-IV program. The different steps in the data processing were:

a. Acquisition and selection of data from each channel.
b. Background subtraction, if any.
c. Calculation of the I-131 overlapping in the Tc-99m channels.
d. Calculation of the heart/kidney correction

factor, F, using the data from the HSA and RBC injections and of the proportionality factor K. (See Appendix: Notations and Abreviations).

e. Calculation of the true [^{131}I] Hippuran and Tc-99m DTPA renal time-activity curves (R(t)) by subtracting the vascular background multiplied by 1/F (see Appendix Eq. 1b).

f. Calculation of the σ slope (see Appendix) by plotting each point on the ascending portion of the true renogram curve as a function of the corresponding value of the heart-curve integral.

g. Calculation of the G/T ratio by using the σ_G and σ_T values and the proportionality factor K.

RESULTS

Uncorrected time-activity curves for the kidney and heart from a representative experiment are shown in Fig. 1. From these data the different correction coefficients are calculated in order to obtain the true renogram and the heart-integral curve.

The calculation of the σ_T and σ_G values is illustrated in Fig. 2. The computer plots the activity of the ascending part of the true renogram curve against the corresponding heart integral at 5-sec intervals. The resulting σ slope is steeper for Hippuran than for DTPA, reflecting the higher Hippuran clearance rate.

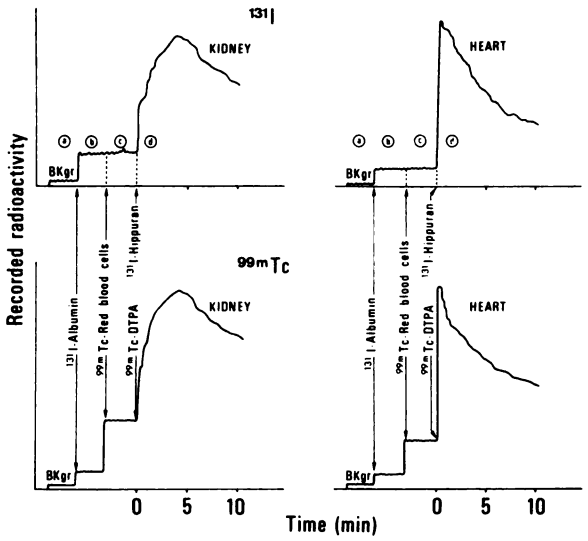

FIG. 1. Diagrammatic presentation of experimental kidney and heart I-131 and Tc-99m time-activity curves from representative experiment: (a) background recording (Bkgr); (b) levels related to I-131 albumin; (c) levels related to Tc-99m red blood cells; (d) [^{131}I] ortho-iodohippurate and Tc-99m DTPA curves.

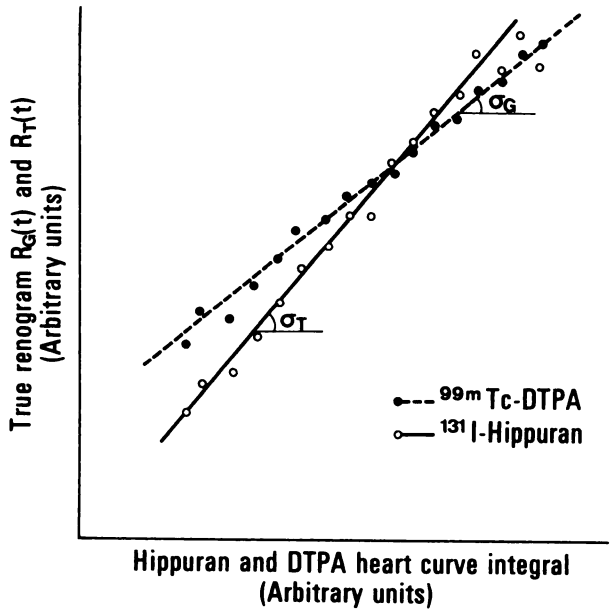

FIG. 2. Calculation of linear coefficient between true renogram R(t) and the corresponding heart integral values for orthoiodohippurate (T) and DTPA (G) during ascending part of kidney curves. Straight lines are obtained by least-squares fitting.

In Table 1, the Tc-99m DTPA and [^{131}I] ortho-iodohippurate clearance values are presented, as well as their ratio, and are compared with the G/T ratio calculated from the early parts of the renograms. As can be seen, the statistical analysis (paired t test) shows no significant difference between the two sets of values. The correlation coefficient is 0.96. The values obtained after Benemid administration are also included in Table 1. Benemid induced a decrease of Hippuran clearance while glomerular filtration rate was not affected. Thus the FF, calculated from the clearance data, increased from the control values of 0.14 and 0.47 to 0.76 and 0.81, respectively, after Benemid administration. The corresponding G/T ratios calculated from the time–activity curves show a similar variation.

Table 2 shows the results obtained after acute ureteral ligation. In the four experiments performed, the glomerular filtration rate was not completely abolished half an hour after ligature but was definitely lower than in control animals. The corresponding ortho-iodohippurate clearance values were only slightly decreased. The resulting clearance ratios and computed G/T ratios were not significantly different in this experiment either.

DISCUSSION

The entire experiment was performed on unilaterally nephrectomized dogs in order to simplify the

TABLE 1. FILTRATION FRACTION MEASURED BY CLEARANCE METHOD (CLEARANCE RATIO) AND BY COMPUTATION (G/T RATIO) IN NORMAL DOGS

Dog No.	Hippuran clearance ml/min	DTPA clearance ml/min	Clearance ratio DTPA/Hippuran X	Computed G/T ratio Y	X — Y d
1	240	84	0.35	0.30	0.05
1*	118	90	0.76	0.82	−0.06
2	159	75	0.47	0.41	0.06
2*	88	72	0.81	0.75	0.06
3	225	81	0.36	0.43	−0.07
4	338	115	0.34	0.38	−0.04
5	350	53	0.15	0.20	−0.05
6	364	51	0.14	0.23	−0.07
7	286	83	0.29	0.21	0.08
8	189	51	0.27	0.17	0.10
	mean		$\bar{X} = 0.394$	$\bar{Y} = 0.390$	$\bar{d} = 0.006$
	Standard deviation				$S_d = 0.069$
	Standard error				$\bar{S}_d = 0.022$
	paired t test $t = \bar{d}/\bar{S}_d$				$t = 0.274$
	$t(9df, \alpha = 5\%) = 2.26$				

No significant difference between the two series of values X, Y

* Clearance measured after tubular blockage with Benemid.

model and make the results of the single-shot clearance measurements strictly comparable with those obtained by external detection. The method may be readily extended to both kidneys in situ.

In order to evaluate renal function from [^{131}I] ortho-iodohippurate and Tc-99m DTPA time–activity curves, we used the early parts of the curves and the blood disappearance kinetics of the tracers to calculate a parameter of renal function, the FF. The early part of the renogram was selected because within the first few minutes, while no tracer has left the kidney via the urinary tract, the renogram is related to the renal and perirenal activity and is proportional to the specific renal accumulation (*1*). We have previously shown that less than 3% of the tracer is excreted into the urine at the time of the renogram peak (*12*). The same pattern was revealed for Tc-99m DTPA (unpublished data). In order to determine the true renogram curve for either [^{131}I] Hippuran or Tc-99m DTPA, a preliminary injection of an intravascular tracer labeled with the corresponding nuclide was needed (*1,14,15*). It was assumed that I-131 HSA and red blood cells labeled with Tc-99m had the same diffusion volume. Labeling albumin with Tc-99m would have been more convenient than red blood cells, but Tc-99m HSA

TABLE 2. FILTRATION FRACTION MEASURED BY CLEARANCE METHOD (CLEARANCE RATIO) AND BY COMPUTATION (G/T RATIO) AFTER URETERAL LIGATURE

Dog No.	Hippuran clearance ml/min	DTPA clearance ml/min	Clearance ratio DTPA/Hippuran X	Computed G/T ratio Y	X — Y d
9	212	11	0.05	0.03	0.02
10	191	6	0.03	0.04	−0.01
11	252	16	0.06	0.08	−0.02
12	226	7	0.03	0.05	−0.02
	mean		$\bar{X} = 0.042$	$\bar{Y} = 0.050$	$\bar{d} = -0.007$
	Standard deviation				$S_d = 0.019$
	Standard error				$\bar{S}_d = 0.009$
	paired t test $t = \bar{d}/\bar{S}_d$				$t = 0.797$
	$t(3df, \alpha = 5\%) = 3.18$				

No significant difference between the two series of values X, Y

was not sufficiently stable at the time of our experiments and was discarded after testing.

The precordial-area recording, rather than that from the subclavicular fossa, was chosen for the calculation of the renal input function, P(t), to ensure better statistical accuracy. Even though in humans the time–activity curve from the subclavicular fossa more closely resembles the renal fossa post nephrectomy, the error introduced by replacing it with the precordial curve appeared negligible when offset by the improved statistical accuracy of the latter in the dog.

The product of the arteriovenous extraction ratio and the true renal plasma flow ($E \times RPF = ERPF$) is directly proportional to the early part of the true renogram divided by the time integral of the blood–activity curve. This relationship has been shown by Britton and Brown (*1*) and is stated mathematically in Eq. 4. If only one tracer is used, however, the constant of proportionality cannot be found because one cannot measure the vascular volume (V_c) in the field of the subclavicular probe. Equation 4 is applicable for [^{131}I] ortho-iodohippurate as well as for Tc-99m DTPA. With two tracers, therefore, Eq. 4 may be applied for each of them leading to Eq. 4b, in which the vascular volume (V_c) cancels out. Since the detection parameters F_G and F_T are measurable by the preliminary injections of I-131 HSA and Tc-99m RBC, and a proportionality factor K is calculated, we can now transform a nonspecific ratio between two slopes (σ_G and σ_T) into a parameter with physiologic meaning, i.e., the glomerulo–tubular ratio. This ratio between the glomerular filtration rate and the effective renal plasma flow represents the filtration fraction.

The precision of the filtration fraction measurement (G/T ratio) was estimated at ±5%. This is the value obtained during the different curve fittings of the experimental time–activity curves. The other potential source of error for FF (Eq. 6a) could occur during the determination of K if the ratio Tc-99m/I-131 should be too low to allow an accurate subtraction of the overlapping of I-131 in the Tc-99m channel.

Validation of the FF calculation from the early part of the two tracings, i.e., the G/T ratio, has been performed by the simultaneous measurement of the two clearances. The similarity between the two sets of values is maintained when tubular transport of [^{131}I] ortho-iodohippurate is impaired by Benemid injection. Under these experimental conditions [^{131}I] ortho-iodohippurate clearance decreased from 240 and 159 ml/min to 118 and 88 ml/min, respectively, in the two dogs studied, whereas glomerular filtration rate, as measured by Tc-99m DTPA clearance, remained practically unchanged. The similarity was also maintained when glomerular filtration rate was acutely decreased by ureteral ligation. In the 4 dogs tested, the glomerular filtration rate decreased sharply, and the Tc-99m DTPA clearances were at the lower limits measurable by the simplified Blaufox technique (*19*). Simultaneously, the Hippuran clearance decreased by 25% from the average value found in controls. Such a dissociation between glomerular filtration rates and Hippuran clearance has been observed by others and its mechanism extensively studied (*20–22*). The calculated G/T ratios and the measured clearance ratios correlated well.

The present results demonstrate that a glomerulotubular ratio can be obtained for each kidney by a noninvasive method using a dual-nuclide technique and external detection. This ratio represents the filtration fraction, which evaluates the glomerulotubular balance and can be of value in certain pathophysiological conditions such as acute renal failure (where the glomerulo-tubular balance may be acutely disrupted), and in renovascular hypertension. This method, as shown in the mathematical description, does not require any additional assumptions such as those used in methods based on compartmental analysis.

APPENDIX

Notations and Abbreviations

N1 = FF	Filtration fraction = ratio of glomerular filtration rate to effective renal plasma flow.
N2 = c, r	Subscripts referring to cardiac (c) and renal (r) detector, respectively.
N3 = T, G	Subscripts referring to [^{131}I] ortho-iodohippurate (T for tubular secreted) or Tc-99m DTPA (G for glomerular filtered), respectively.
N4 = R(t)	"True renogram," i.e., the time–activity curve corrected for blood background activity.
N5 = R(t)	Observed renogram.
N6 = P(t)	Time–activity curve recorded from precordial area.
N7 = C(t)	Concentration of tracer in the renal artery at time t, i.e., the "true input function." Note units are activity per unit volume.
N8 = τ	Heart-to-kidney transit time, i.e., the time required for a bolus of tracer to travel from the heart to the renal artery.
N9 = RPF	Renal plasma flow.
N10 = E_T, E_G	Renal arteriovenous extraction ratios for tubular (T) and glo-

merular (G) type tracers, respectively.

N11 a = $(ERPF)_T$ — Effective renal plasma flow for a tubular-type tracer. Since effective renal plasma flow is defined as the product of extraction ratio E times RPF, then E × RPF = ERPF.

N11 b = $(ERPF)_G$ — For notational consistency, the symbol $(ERPF)_G$ has been maintained even when a glomerular type tracer was used. It in fact corresponds to the glomerular filtration rate and not to the effective renal plasma flow in the usual sense.

N12 = T_{max} — Time corresponding to the peak of the renogram or "renal transit time."

N13 = ϵ_c, ϵ_r — Efficiency of the cardiac (c) and renal (r) detector, respectively.

N14 = V_c, V_r — Vascular volume in the field of view of the cardiac or renal detectors, respectively.

N15 = $F \equiv \frac{\epsilon_c}{\epsilon_r}\frac{V_c}{V_r}$ — Note that F now contains all the parameters related to external detection, i.e., probe efficiency and vascular volume seen by each probe (*1*). F is directly measurable after injection of intravascular tracers: Tc-99m RBC and I-131 HSA. The notation is F_G and F_T, respectively.

N16 = $K \equiv \frac{F_G}{F_T}$

N17 = $\sigma \equiv \frac{R(t)}{\int_0^t P(\theta - \tau)d\theta}$ — Represents the angular coefficient of the straight line obtained by least-squares fitting of R(t) compared with $\int_0^t P(\theta - \tau)d\theta$*.

N18 = $\frac{G}{T} = \frac{E_G}{E_T} = FF$ — G/T the final product of this analysis is the ratio of the extraction ratios for Tc-99m DTPA and [^{131}I] ortho-iodohippurate. G/T ratio is equal to the filtration fraction.

Theoretical Analysis

The true renogram may be obtained in a subject with a unilateral nephrectomy by subtracting the time-activity curve for the nephrectomy bed (the "nephrectomy trace") from the renogram obtained from the contralateral kidney. Further, it has been shown that the nephrectomy trace may be closely approximated by a detector viewing the subclavicular area (SCA)† (*2,3*).

$$\text{true renogram} = \text{observed renogram} - \text{nephrectomy trace}, \quad (1)$$

where nephrectomy trace = SCA trace.

While Eq. 1 is qualitatively correct, it cannot be expressed in precise mathematical terms unless appropriate scale factors are introduced to correct for detector efficiencies and dimensional consistency. For example, if in Eq. 1 the true renogram has units of activity per milliliter, all other terms must have identical units.

Detector efficiency corrections: if a detector views an area with an efficiency ϵ, then the actual activity in the field of view of the detector is calculated by dividing the observed activity by ϵ.

Dimensional corrections: we express each term in Eq. 1 in units of activity of tracer per unit volume. The activity A from a source of volume V may be expressed on a unit volume basis as A/V. Thus Eq. 1 may be expessed as

$$\frac{R(t)}{\epsilon_r V_r} = \frac{R(t)}{\epsilon_r V_r} - \frac{P(t-\tau)}{\epsilon_c V_c} \quad (1a)$$

Where τ (see N8) corrects for the time lag between heart and kidney during the first few circulations (see N2, N4, N13, and N14).

Rearranging Eq. 1a and using N15,

$$R(t) = R(t) - \frac{\epsilon_r V_r}{\epsilon_c V_c} P(t-\tau) = R(t) - \frac{1}{F} \cdot P(t-\tau) \quad (1b)$$

F, the heart/kidney correction factor, is determined after the injection of an intravascular tracer (*10,12*). After a few minutes for equilibration, F is calculated by dividing the activity observed by the precordial detector P by the activity observed by the renal detector *R*. Thus, F = P/R*.

The ensuing renogram is now corrected with complete subtraction of vascular background.

Estimation of the true input function C(t): the precordial detector views the great vessels (or heart) and it is assumed that the amount of tracer in the mediastinal interstitium is negligible. With this assumption, P(t) is proportional to plasma activity.

Correcting for detector efficiency, vascular volume and time lag, we may write:

$$C(t) = \frac{1}{\epsilon_c V_c} P(t-\tau). \quad (2)$$

The rate at which tracer enters the kidney depends on RPF, extraction ratio E, and plasma concentration of tracer C(t). Since it is assumed that no tracer leaves the kidney before T_{max} (see N12) the kidney acts as a collecting reservoir (or integrator) of tracer entering via the renal artery. Thus, tracer enters at a rate equal to E · RPF · C(t) and at time $t \leq T_{max}$ the amount of tracer in the kidney is (see N11):

$$\int_0^t ERPF \cdot C(\theta)d\theta.$$

* θ represents the dummy variable of integration.

† We have chosen to approximate this activity from the precordial rather than the subclavicular area because of the superior counting statistics of the former, although a slight error is introduced during the first circulation of tracer since the detector views both the right and left heart.

* The rationale for the calculation of F may be understood by examination of Eq. 1b. After injection of only the intravascular tracer, activity measured by the renal detector is due only to tracer in the vascular space and not renal function activity. Thus the non-vascular renal activity (R(t)) equals zero. Since measurements are made after the equilibration of tracer, R and P are independent of time and we may write as:

$$R = 0 = R - \frac{1}{F} \cdot P \text{ or } F = \frac{P}{R}$$

Since the kidney detector views this activity with an efficiency ϵ_r,

$$R(t) = \epsilon_r \int_0^t ERPF \cdot C(\theta)d\theta. \quad (3)$$

Combining Eqs. 2 and 3 and rearranging

$$ERPF = \frac{\epsilon_c V_c}{\epsilon_r} \cdot R(t) \frac{I}{\int_0^t P(\theta - \tau)d\theta}. \quad (4)$$

Using N17, we obtain

$$ERPF = \frac{\epsilon_c V_c}{\epsilon_r} \cdot \sigma. \quad (4a)$$

If we simultaneously use a tubular and a glomerural tracer with different extraction ratios E_T and E_G, different photon energies with detector efficiencies ϵ_T, ϵ_G, and noting that vascular volumes are only a function of detector geometry and not of photon energies, we may write:

$$\frac{E_G}{E_T} = \frac{E_G \cdot RPF}{E_T \cdot RPF} = \frac{(ERPF)_G^*}{(ERPF)_T}$$

$$= \left(\frac{\epsilon_c}{\epsilon_r}\right)_G \cdot \left(\frac{\epsilon_c}{\epsilon_r}\right)_T^{-1} \cdot \frac{\sigma G}{\sigma T}. \quad (4b)$$

From N15

$$\frac{F_G}{F_T} = \left(\frac{\epsilon_c V_c}{\epsilon_r V_r}\right)_G \left(\frac{\epsilon_c V_c}{\epsilon_r V_r}\right)_T^{-1}$$

$$= \left(\frac{\epsilon_c}{\epsilon_r}\right)_G \left(\frac{\epsilon_c}{\epsilon_r}\right)_T^{-1}. \quad (5)$$

As mentioned in the discussion of formula 1, F_T and F_G are easily measured parameters. Now combining Eq. 5 with Eq. 4b we have

$$\frac{E_G}{E_T} = \frac{F_G}{F_T} \cdot \frac{\sigma_G}{\sigma_T} \quad (6)$$

Substituting N16, N18, and N19, we obtain the final simple relationship

$$FF = \frac{G}{T} = K \frac{\sigma_G}{\sigma_T} \quad (6a)$$

To summarize:

1. The first step involves the determination of the true renograms for both [^{131}I] ortho-iodohippurate and Tc-99m DTPA. During this step a factor (F) is determined that includes all the cumbersome parameters related to detection (geometry, efficiency, absorption).
2. The next step is based upon the following:
   a. The true renogram is dependent upon Effective Renal Plasma Flow (ERPF), tracer concentration in the renal artery, and detector factors.
   b. ERPF is directly proportional to both the tracer's extraction ratio and renal plasma flow, RPF. By using the available equations, an expression is sought for the ratio whose numerator is the extraction ratio for DTPA and the denominator that for ortho-iodohippurate.

By simple mathematical manipulations it is shown that all the remaining parameters either cancel out or can be easily measured. Thus the end result is a number representing a parameter with pathophysiologic significance, i.e., the G/T ratio. This value is also equal to the Tc-99m DTPA/[^{131}I] ortho-iodohippurate clearance ratio or the filtration fraction.

* To ensure a clearer understanding of the transition from formula 4a to 4b and notational consistency, we have used the symbol $(ERPF)_G$ even though it is physiologically a misnomer. It in fact corresponds to glomerular filtration rate. (see N11 b)

FOOTNOTE

* Benemid®: di-n-propylsulfamyl benzoic acid.

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