Technetium-99m DTPA Renal Flow Studies in Goldblatt Hypertension

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Computer-assisted dynamic renal studies were performed on a group of 14 mongrel dogs before and after the induction of unilateral renal artery stenosis. Ninety-second technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA), 15-min [^{99m}Tc]DTPA, and 30-min iodine-131 orthoiodohippurate ([^{131}I]hippuran) time-activity curves were analyzed and correlated with reduction of renal blood flow as measured by electromagnetic flow probe and PAH clearance techniques. Parameters of the 90-sec [^{99m}Tc]DTPA curves found to be significantly different for the same kidney before and after stenosis were: upslope, curve width at 75% maximum, maximum activity value, and differential (stenotic/contralateral) maximum activity ratio. For blood flow reductions greater than 33%, the [^{99m}Tc]DTPA studies were judged diagnostic of unilateral renal artery stenosis in all cases, whereas the [^{131}I]hippuran time-activity curves were indicative of stenosis in only six of ten studies. Thus, in this model we find the computer-assisted 90-sec [^{99m}Tc]DTPA renal flow study to be superior to conventional [^{131}I]hippuran renography in the diagnosis of moderate-to-severe unilateral renal artery stenosis.

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Although radionuclide assessment of the kidney is playing an increasingly larger role in the diagnosis of renal disease, debate continues over its utility in the evaluation of renal vascular hypertension (RVHT). Controversy exists because of the relatively low prevalence of RVHT (2–5%) in the general hypertensive population coupled with the suboptimal results obtained with conventional iodine-131 orthovodohippurate ([^{131}I]hippuran) renography. Although this test may detect up to 75–85% of patients with RVHT (range 67–98%), reports have usually noted 10–20% false-positive rate in the essential hypertension population (*1–3,8*). Data with these degrees of sensitivity and specificity result in a fairly low predictive value for a positive test when applied to a subset of hypertension with a low prevalence (*4*). These observations, plus cost effectiveness issues, understandably underlie the controversy regarding the role of conventional renography in the diagnosis of RVHT.

Conventional [^{131}I]hippuran renography has been somewhat limited because of the variability of diagnostic patterns in patients with renovascular hypertension. Classically, the most useful pattern is decreased and prolonged accumulation and excretion of the radionuclide seen on the stenotic side. However, virtually any pattern from prolonged uptake and excretion of [^{131}I]hippuran to a markedly depressed renogram with a severe reduction of renal blood flow and radionuclide delivery to the kidney may be observed in RVHT (*17*). Renal parenchymal disease and ureteral obstruction may also result in patterns initially thought to be diagnostic of RVHT such that its specificity has also been called into question. Although [^{131}I]hippuran serves as an excellent marker for detecting reduced functioning renal tissue, it has a complex renal excretion by both glomerular filtration and active tubular secretion. This, combined with the suboptimal imaging characteristics of ^{131}I, limits its usefulness as an acceptable screening test for renovascular hypertension, especially in patients with renal dysfunction.

Radiopharmaceuticals such as technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) appear promising as useful agents to assess renal perfusion because of their lower radiation dose, shorter half-life, and the high detection efficiency needed for good quality rapid sequence gamma camera imaging (*5*). Dynamic renal imaging with [^{99m}Tc]DTPA over 30

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min has been reported by others to be a good screening test for RVHT (*6*). We have previously reported the development of a 90 sec, computer-assisted [^{99m}Tc]DTPA renal perfusion study in a preliminary group of patients with angiographically-proven renovascular hypertension and preserved renal function (*7*). These studies demonstrated consistent, uniform changes in curve height and configuration of the 90-sec time-activity curves of the stenotic kidneys. While pursuing these clinical observations, we were also concerned about the potential impact of co-existing pathology such as renal artery stenosis, glomerular nephrosclerosis, and tubulo-interstitial damage upon the [^{99m}Tc]DTPA time activity curves. Therefore, we elected to evaluate further the 90-sec and 15-min [^{99m}Tc]DTPA scan techniques and compare them to conventional [^{131}I]hippuran renography in an experimental canine model of two kidney, one-clip Goldblatt hypertension.

MATERIALS AND METHODS

Experimental protocol

Studies were performed in female mongrel dogs (n = 14) who were known to have single normal renal arteries from previous angiography. During the control period, the animals were anesthetized with pentobarbital (30 mg/kg) and a conventional clearance study with paraaminohippurate (PAH) by way of a bladder catheter and blood pressure determinations through a femoral artery catheter were performed. On another day, the anesthetized animals were hydrated to insure a urine output of greater than 2 cc/min, and they then underwent the [^{99m}Tc]DTPA studies followed by a 30 min [^{131}I]hippuran renogram (see Nuclear studies).

During the renal artery stenosis period, the animals were again anesthetized and the left renal artery was approached anteriorly. An electromagnetic flow probe (EMFP) was placed and measurements of unilateral renal flow were taken after a stabilization period. A metallic surgical clip was then positioned proximal to the EMFP to approximate a 50% reduction in renal blood flow. On the following day, the well hydrated animals then again underwent [^{99m}Tc]DTPA and [^{131}I]hippuran studies. The next day, the animals underwent split-function PAH clearance studies with urine collection through individual ureteral catheters. A post-study angiogram and blood pressure determinations were also performed.

Following the completion of the studies, the data were grouped on the basis of the results of the split-function PAH clearances as a measure of the degree of left renal artery stenosis. Those animals in Group I (n = 10) had a moderate-to-severe stenosis with greater than 30% (range 33–99%) reduction in PAH clearance. Those animals in Group II (n = 4) had a mild stenosis with less than a 25% reduction.

Nuclear studies

For the [^{99m}Tc]DTPA study, 5 mCi [^{99m}Tc]DTPA was injected rapidly by way of the cephalic vein with the animal lying supine and the anatomy viewed posteriorly by a large field of view gamma camera* using a medium energy collimator. Data were acquired by a PDP 11/34 computer† using a predefined study routine operating under gamma 11 and RT-11 software. Data acquisition was formulated into a 64 × 64 pixel matrix. The dynamics of the [^{99m}Tc]DTPA study were specified by a collection time of 1 sec per frame for 90 sec, then 10 sec/frame for 13.5 min for a total of a 15 min study.

The regions of interest were selected to include the aorta, left and right kidneys, and corresponding background areas to be subtracted. These time-activity curves, which are generated, then serve as input for our analysis programs. A separate time activity curve for the aortic region is plotted in order to assess the quality of bolus at the main renal arteries. A poor, staggered aortic curve was a potential criterion for rejecting the study. The time-activity curve for the left and right kidneys were plotted on the same set of axes with the activity scale normalized to the higher kidney's peak activity. This display format facilitates direct bilateral comparison.

Eight computer-isolated curve parameters were analyzed from the 90-sec [^{99m}Tc]DTPA renal flow study. These are schematically illustrated in Fig. 1 with the exception of the left/right maximum activity ratios. These parameters include: (a) maximum activity (counts); (b) upslope (%/sec); (c) rise time (sec); (d) time to maximum activity ($T_{max, sec}$); (e) backslope (%/sec); (f) left/right maximum activity ratios; (g) min/max ratio; and (h) the curve width at 75% maximum (sec). A computer-generated normal kidney template was also derived from data from the normal kidneys during the control period. This template was generated by aligning the peaks and averaging over the 28 normal kidneys. The pairs of time-activity curves from the 90-sec and 15-min [^{99m}Tc]DTPA renal flow studies were also visually analyzed for configuration, slope, and symmetry. These studies were defined as normal if both kidney curves had virtually identical curve height and configuration such that they were able to be superimposed upon one another (i.e., less than 15% variability). Curves from the stenotic kidney were considered diagnostic if there was a greater than 25% reduction in curve height and asymmetry of curve configuration compared to the contralateral kidney. The curve parameters for an individual kidney were compared before and after the creation of renal artery stenosis for both the stenotic kidney and the contra-

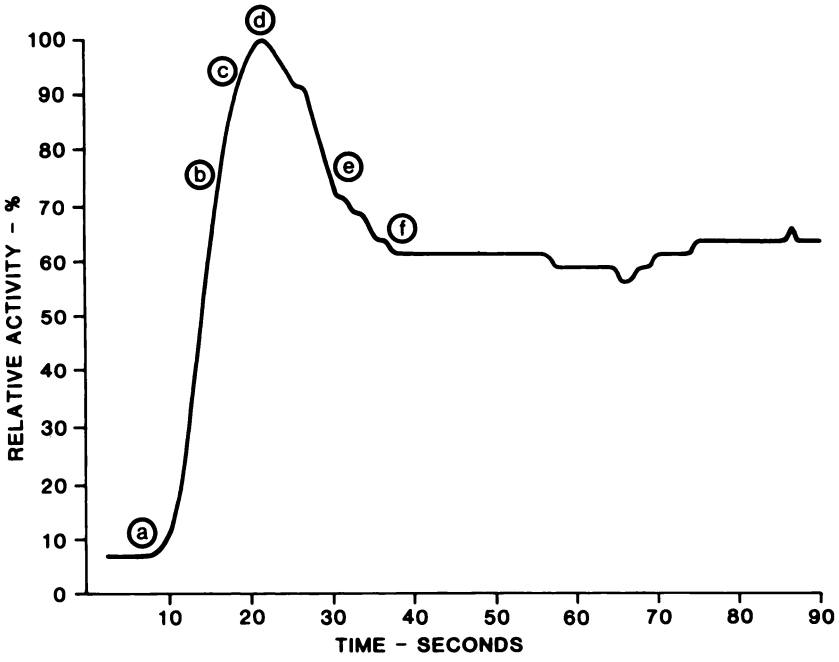

FIGURE 1
Illustration of 90-sec [^{99m}Tc]DTPA computer isolated curve parameters. Maximum value (counts) (d); Up-slope from 5% to 90% (%/sec) (a) to (c); Rise time from 5% to 90% (sec) (a) to (c); Time from 50% to maximum value (sec) (a) to (d); Time from maximum to first minimum (sec) (d) to (f); Backslope from maximum to first minimum value (%/sec) (d) to (f); Ratio of first minimum to maximum value (%) (f)/(d); Full width of curve at three quarters of maximum value (sec) (b) to (e)

lateral kidney. In addition, curve parameters were analyzed following renal artery stenosis for the stenotic in comparison with contralateral kidneys. Studies were determined to be diagnostic on the basis of visual analysis coupled with quantitative assessment of curve parameters.

The 30-min [^{131}I]hippuran renograms were completed using the same gamma camera and collimator as described for the ^{99m}Tc-DTPA studies above. The regions of interest were selected for each kidney and the bladder with background regions for subtraction. The [^{131}I]hippuran dose was selected to be 40 μCi i.v. for these experimental dog studies such that this activity provided count rates comparable to our human studies and resulted in target-to-background ratios exceeding 5:1 for adequate statistical analysis. The time activity curves were analyzed in the conventional manner (*8*) with respect to time to maximum activity, time to return from maximum of 75% maximum activity, upslope, backslope, and the differential (stenotic/contralateral) maximum activity ratios. These curves were also subjected to visual analysis and interpretation. The criteria for a normal study included a sharp peak within the first 2 min, cross over with the bladder curve between 4–8 min, and return to baseline within 15 min. Again, symmetry of curve upslope, backslope and overall shape (i.e., less than 15% variability) was imperative for a study to be considered normal. Marked asymmetry between the individual kidney curves was a hallmark for the diagnostic criteria for renal artery stenosis. Significant variation in curve configuration exists following stenosis so that either prolonged accumulation and excretion or a markedly depressed time activity curve were considered consistent with renal artery stenosis.

The results are expressed as a mean ± s.e.m. Statistical analysis was accomplished by use of the paired and unpaired Students' t-tests (*9*).

RESULTS

The results of the visual interpretation of the [^{99m}Tc]DTPA and [^{131}I]hippuran time-activity curves performed on all the normal animals in the control period can be found in Table 1. As can be seen from Table 1, 13 of 14 (92.8%) of both the 90-sec computer-assisted [^{99m}Tc]DTPA renal flow study and the 15-min [^{99m}Tc]DTPA study were considered to be normal. However, only 10 of 14 (71.4%) of the conventional [^{131}I]hippuran time-activity curves were judged to be within normal limits according to the predefined criteria.

Figure 2 illustrates the computer-generated normal kidney template from the 90-sec [^{99m}Tc]DTPA renal flow study obtained from the normal kidneys. Curve parameters ± s.e.m. from the 90-sec [^{99m}Tc]DTPA normal studies are represented in Table 2. There were

TABLE 1
Visual Interpretation of Control Nuclear Studies

Item	Time	Normal Studies
[^{99m}Tc]DTPA	90 sec	13/14
	15 min	13/14
[^{131}I]hippuran	30 min	10/14

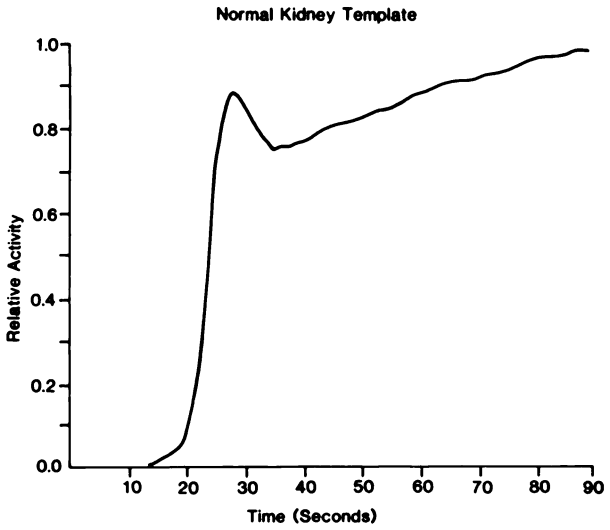

FIGURE 2
Computer generated normal kidney template formed from the control 90-sec [^{99m}Tc]DTPA renal flow studies

no significant differences in curve parameters between left and right kidneys in the control period. The normal template was then utilized subsequently to compare curve configuration and curve parameters following unilateral renal artery stenosis.

Creation of unilateral renal artery stenosis in Group I animals resulted in a 57.8 ± 9.3% reduction in ipsilateral renal blood flow (range 33–99%) as measured by split-function PAH clearances performed two days after surgery. The average reduction measured at the time of surgery by EMFP was 52.4 ± 2.7% for an agreement of r = 0.833 with the two different determinations. Mean arterial pressure increased significantly from 135.9 ± 3.3 to 151.8 ± 3.5 mm Hg following renal artery stenosis ($p < 0.005$). In contrast, the four animals in Group II had only a 10% stenosis on average (as assessed by C_{PAH}) and an inconsistent elevation of mean arterial pressure.

Results of the visual interpretation for the [^{131}I]hippuran renograms, the 90-sec [^{99m}Tc]DPTA renal flow studies, and the 15-min [^{99m}Tc]DTPA studies for Groups I and II following renal artery stenosis can be found in Table 3. As can be seen from Table 3, the computer-assisted 90-sec [^{99m}Tc]DTPA renal flow studies were considered diagnostic in all ten of the animals in Group I studied following renal artery stenosis. Upon visual analysis, there were uniform alterations in both curve height and configuration, as illustrated in Fig. 3 from Dog E studied before (left) and after (right) creation of left renal artery stenosis. The uniformity of the changes with the 90-sec [^{99m}Tc]DTPA renal flow study following renal artery stenosis are in contrast to the variability of the [^{131}I]hippuran renograms which exhibit either depressed or hyperconcentrated curve forms following renal artery stenosis.

TABLE 2
Normal Kidney Template Parameters of the 90-sec [^{99m}Tc]DTPA Curves

Maximum value (counts)	711 ± 58
Upslope from 5% to 90% (%/sec)	12.03 ± 0.52
Rise time from 5% to 90% (sec)	7.11 ± 0.19
Time from 5% to maximum value (sec)	9.32 ± 0.32
Time from maximum to first minimum (sec)	8.79 ± 0.51
Ratio of the first minimum to the maximum value (%)	71.21 ± 1.6
Backslope from maximum to first minimum value (%/sec)	3.61 ± 0.28
Full width of the curve at three quarters of the maximum value (sec)	9.95 ± 1.0

The eight parameters of the 90-sec [^{99m}Tc]DTPA time-activity curves of the stenosed kidney from Group I are listed in Table 4. The curve parameters of the stenosed kidney found to be significantly different from the curve generated from that same kidney during the control period were: (a) upslope ($p < 0.02$); (b) curve width at 75% maximum ($p < 0.02$); (c) maximum activity value ($p < 0.01$); and, (d) the differential (stenotic/contralateral) maximum activity ratios ($p < 0.001$). When comparing the post-stenotic curve parameters from the contralateral kidney back to itself during the control studies, there was a significant increase in maximum activity value ($p < 0.02$) and curve width ($p < 0.05$) suggesting an increase in the delivery of radionuclide to the contralateral kidney following the stenosis. In comparing the stenotic kidney to the contralateral kidney after stenosis significant differences were found between the maximum activity value ($p < 0.003$) and the differential (stenotic/contralateral) maximum activity ratios ($p < 0.001$). Curve slope and width were no longer significant with this comparison because of an increase in curve height and width in the contralateral kidney following stenosis.

The time-activity curves from the 15-min [^{99m}Tc]DTPA study were also considered to be diagnostic of unilateral renal artery stenosis in all 10 animals of Group I. All of the curve forms were significantly depressed in a uniform manner with the maximum activity value of approximately 45% compared to the

TABLE 3
Visual Interpretation of Nuclear Studies Following Stenosis

Item	Diagnostic Studies		Time
	Group I	Group II	
[^{99m}Tc]DTPA	10/10	1/4	90 sec
	10/10	2/4	15 min
[^{131}I]hippuran	6/10	6/4	30 min

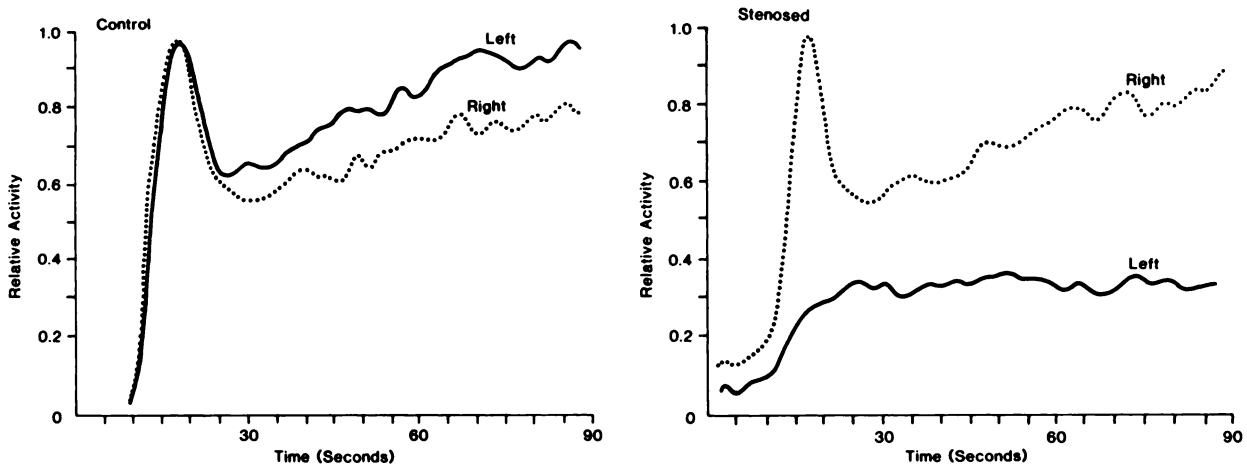

FIGURE 3
Left: Control 90-sec [^{99m}Tc]DTPA renal flow study in Dog E. Right: 90-sec [^{99m}Tc]DTPA renal flow study following left renal artery stenosis in Dog E

contralateral curve. There were significant changes in curve upslope and backslope, but no significant delay in time to maximum activity.

The conventional 30-min [^{131}I]hippuran time-activity curves were diagnostic in six of 10 cases in Group I as judged by the predetermined criteria. In three, the curves of the stenotic kidney were markedly depressed, whereas, three other poststenotic curves exhibited a significant accumulation of radionuclide with delayed accumulation and excretion suggestive of hyperconcentration of urine within the stenotic kidney. The four remaining curves were quite variable regarding curve height and configuration and were considered nondiagnostic of renal artery stenosis. As seen in Table 5 for Group 1, curve upslope was decreased and time to maximum activity was significantly delayed. However, curve shape was highly variable with no significant differences in differential (stenotic/contralateral) maximum activity ratios so that visual diagnostic interpretation was often limited.

In Group II, the [^{131}I]hippuran renogram was not suggestive of renal artery stenosis in any of the four animals. The 90-sec [^{99m}Tc]DTPA renal flow study was suggestive of unilateral renal artery stenosis in one of four animals. The 15-min [^{99m}Tc]DTPA time activity curve was depressed on the "stenotic" side in two of four animals.

DISCUSSION

The computer-assisted 90-sec [^{99m}Tc]DTPA renal flow study appears to be superior to the conventional [^{131}I]hippuran renogram in detecting unilateral renal artery stenosis in our acute canine model of two-kidney, one-clip Goldblatt hypertension. Creation of moderate to severe unilateral renal artery stenosis resulted in

TABLE 4
Curve Parameters of the 90-sec [^{99m}Tc]DTPA Study of the Stenotic Kidney Before and After Stenosis in Group I

Item	Pre-stenosis	Post-stenosis	Activity value
Maximum value (counts)	808 ± 111	450 ± 67	$p < 0.01$
Upslope from 5% to 90% (%/sec)	13.29 ± 0.52	9.19 ± 1.0	$p < 0.02$
Rise time from 5% to 90% (sec)	6.6 ± 0.27	8.5 ± 0.79	p = N.S.
Time from 5% to maximum value (sec)	8.4 ± 0.40	10.6 ± 0.81	p = N.S.
Time from maximum to first minimum (sec)	10.0 ± 1.0	9.7 ± 3.7	p = N.S.
Backslope from maximum to first minimum value (%/sec)	3.44 ± 0.42	3.35 ± 0.60	p = N.S.
Ratio of the first minimum to the maximum value (%)	68.88 ± 2.2	79.8 ± 3.7	p = N.S.
Full width of the curve at three quarters of the maximum value (sec)	8.39 ± 1.7	44.5 ± 13	$p < 0.02$
Differential (stenotic/contralateral) maximum activity ratio	1.11 ± 0.06	0.45 ± 0.06	$p < 0.001$

TABLE 5
Curve Parameters of the [^{131}I]Hippuran Renogram of the Stenotic Kidney Before and After Stenosis in Group I

Item	Pre-stenosis	Post-stenosis	Activity value
Time to maximum (sec)	1.37 ± 0.32	7.17 ± 1.8	$p < 0.01$
Time to return to 3/4 maximum (sec)	2.83 ± 0.49	11.1 ± 2.8	$p < 0.02$
Upslope (%/sec)	51.4 ± 4.3	19.2 ± 7.0	$p < 0.001$
Backslope (%/sec)	17.4 ± 1.9	10.1 ± 2.4	p = N.S.
Differential (stenotic/contralateral) maximum activity ratio	0.96 ± 0.10	0.67 ± 0.12	p = N.S.

uniform alterations of curve height and configuration of the 90-sec time-activity curve of the stenotic kidney with significant changes in curve upslope, curve width, and differential (stenotic/contralateral) maximum activity ratios. In addition, there appeared to be compensatory changes in the contralateral kidney with an increase in curve height and width suggestive of the physiological increase in renal blood flow of the contralateral kidney documented with acute models of unilateral renal artery stenosis (*10*). In contrast to the [^{99m}Tc]DTPA studies, there was considerable variability in the conventional [^{131}I]hippuran time-activity curves in both the control studies and those following stenosis. Although there was a significant delay in time to maximal activity and a decrease in curve upslope (aided by the presence of three flat curves following stenosis), there was a tremendous degree of variability in curve configuration and differential (stenotic/contralateral) maximum activity ratios. Overall, the [^{131}I]hippuran renogram was considered to be of more limited value in the detection of renal artery stenosis in our model.

Conceptually, assessment of renal blood flow with [^{131}I]hippuran has been an attractive hypothesis. Ortho-iodohippurate (OIH) is excreted by the kidneys in a fashion similar to PAH, mostly by active tubular secretion (80%) and much less by glomerular filtration (20%). Iodine-131 has the characteristics of a longer physical half-life and less advantageous imaging characteristics when compared to technetium-labeled compounds (*5*). However, the more rapid biological half-life of OIH in patients with nearly normal renal function may result in less radiation exposure to whole body and kidneys for those individuals (*17*). OIH excretion is highly dependent upon active tubular transport within the kidney and this variable, especially in those patients with renal hypoperfusion created by renal artery stenosis, could result in different accumulation and excretion patterns thus rendering interpretation of renal perfusion difficult. Perhaps the best clinical utility of the OIH renogram in renovascular hypertension may be the ability to detect the presence of functional renal tissue when other modalities simply identify a small, shrunken kidney. Similarly, the OIH renogram may have utility in evaluating renal parenchymal disease with its attendant problems with secondary hypertension. Studies with iodine-123 hippuran [(^{123}I]hippuran), a radionuclide providing less radiation dose and better imaging characteristics, have demonstrated accurate quantitation of effective renal plasma flow in patients with renal artery stenosis (*11*). However, [^{123}I]hippuran is currently expensive and not widely available (*12*).

More recent studies suggest that [^{99m}Tc]DTPA may be a more suitable radionuclide for the assessment of the renal hypoperfusion in renovascular hypertension. Technetium-99m-labeled compounds appear to have superior detection efficiency required for better quality rapid sequence gamma camera imaging which lends itself to computer analysis (*5*). We specifically examined the bolus arrival of the [^{99m}Tc]DTPA to the kidney during the initial 90 sec following injection to serve as a marker of renal perfusion. Analysis of the aortic bolus time-activity curve derived from regions of interest in the abdominal aorta above the renal arteries served as a criterion of input function for this model. This assessment of the input function remains crucial in order to interpret the early passage of the [^{99m}Tc]DTPA into the renal vascular beds. All animals whose [^{99m}Tc]DTPA kidney time-activity curves were evaluated had acceptable aortic bolus time-activity curves in order to be included for analysis. Otherwise, a staggered arrival of the radionuclide into the aorta would result in a broad aortic input function which could result in increased convolution of the kidney time activity curves (*18*).

In our study with acute unilateral renal artery stenosis, the 90-sec [^{99m}Tc]DTPA renal flow study was diagnostic in all animals in Group I with significant stenosis. Stenosis resulted in uniform alterations of both the 90-sec and 15-min [^{99m}Tc]DTPA time-activity curves with depressed curve height and slope. These unidirectional changes contrasted with the variability of either prolonged accumulation or marked depression of the time-activity curves experienced with the OIH renograms following renal artery stenosis. This consistency with the [^{99m}Tc]DTPA renal flow studies made interpretation more readily reproducible since more rigid diagnostic criteria could be established for unilateral renal artery stenosis from analysis of this model. These same

diagnostic criteria with minor modifications are being successfully applied to our [^{99m}Tc]DTPA renal flow studies in patients with angiographically proven renal artery stenosis (*7*).

Employing the time-activity curve data gathered from the normal kidneys, we were also able to generate a normal kidney template for the 90-sec [^{99m}Tc]DTPA renal flow study. The mean ± s.e.m. values of curve parameters were compiled from this template. The configuration and range of parameter values of this normal template from our experimental animal model is in close agreement with the normal template our group has established for human volunteers (*13*). It is felt that the development of a normal template is extremely helpful as a standard for comparison of subsequent curves of experimental animals or patients who may have unilateral or bilateral renovascular disease. The utility of the normal template may be greatest in patients with bilateral disease since interpretation of any screening diagnostic modality is hampered if asymmetry alone is required as an important diagnostic criterion. It is this selective patient population with bilateral RVHT that may present with refractory hypertension and azotemia that may greatly benefit from detection and correction of their problem (*18*). Ironically, detection of these patients suffers since the sensitivity and specificity of the rapid sequence IVP in bilateral renal artery stenosis is more limited. It is hoped that comparison of these 90-sec [^{99m}Tc]DTPA time-activity curves to the normal template will enhance the diagnostic ability within this patient population. In addition, further analysis and curve-modeling of the 90-sec time-activity curves compared to results of classic clearance studies representing renal blood flow and glomerular filtration rate may eventually result in a quantitative assessment of renal perfusion and function from the 90-sec [^{99m}Tc]DTPA renal flow curves without requiring the sampling of blood or urine (*19*).

These studies suggest that [^{99m}Tc]DTPA renal flow studies are more sensitive than conventional OIH renography in detecting acute reductions in renal blood flow. However, the specificity of the [^{99m}Tc]DTPA studies remains in question. Studies performed in well-hydrated animals during the control period were deemed to be normal in 13 of 14 studies for a false-positive rate of only 1 of 14 (7%). These data contrast with the 28% false-positive rate (4 of 14) during the control period with the [^{131}I]hippuran renogram and its more limited diagnostic accuracy in detecting renal artery stenosis (6 of 10 in Group I). The sensitivity and specificity of the 90-sec [^{99m}Tc]DTPA renal flow study in our animal model is in general agreement with the results reported by our group (*13*) and others (*6*) in patients with renovascular hypertension and/or normal individuals. Further studies are obviously needed in subjects with urinary tract obstruction or other forms of parenchymal renal disease for additional evaluation of sensitivity and specificity criteria. The marginal results obtained in the small number of animals in Group II with mild stenosis are difficult to interpret with confidence regarding the sensitivity or specificity of the [^{99m}Tc]DTPA studies or the degree of stenosis required to be considered causative in maintaining renovascular hypertension. It is believed that combining the computer-assisted [^{99m}Tc]DTPA renal flow studies with the pharmacological blockade of the renin-angiotensin system using the physiological challenge of converting enzyme inhibition as reported by us (*14*) and others (*15,16*) may aid in the noninvasive diagnosis of renovascular disease in these and other problematic cases. These radionuclide assessments of renal blood flow can be accomplished without subjecting the patient with renal disease to the potential nephrotoxicities of radiocontrast materials, as well as allowing for the greater ease of the procedure for both patients and staff. These advantages of the combination of the [^{99m}Tc]DTPA studies with Captopril challenge and the less toxic noninvasive nature of the procedure will allow us to document either the natural history of RVHT or the effects of interventional surgery or angioplasty. These observations should result in a better understanding of the pathophysiology of RVHT and improved methods of detection and therapy.

In summary, the computer-assisted 90-sec [^{99m}Tc]DTPA renal flow study appears to be superior to conventional [^{131}I]hippuran renography in the diagnosis of moderate-to-severe unilateral renal artery stenosis. A normal template was generated from control kidneys and diagnostic criteria for unilateral renal artery stenosis with consistent, uniform changes in curve height and configuration have been established. The potential exists for further analysis of the 90-sec [^{99m}Tc]DTPA time-activity curves which may result in a noninvasive quantitative assessment of renal perfusion and function. Combination of these computer-assisted [^{99m}Tc]DTPA renal flow studies with the physiological challenge of angiotensin converting enzyme inhibition may also offer promise in the noninvasive radionuclide assessment of renovascular hypertension.

FOOTNOTES

* Maxicamera II, General Electric.
† Digital Equipment Corp.

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REFERENCES

1. Arlart I, Rosenthal J, Adam WE, et al: Predictive value of radionuclide methods in the diagnosis of unilateral renovascular hypertension. *Cardiovasc Radiol* 2:115–125, 1979
2. McNeil BJ, Varady PD, Burrows BA, et al: Cost-effectiveness calculations in the diagnosis and treatment of hypertensive renovascular disease. *N Engl J Med* 293:216–221, 1975
3. Hunt JC, Strong CG, Sheps SG, et al: Diagnosis and management of renovascular hypertension. *Am J Cardiol* 23:434–445, 1969
4. Keim HJ, Johnson PM, Vaughan ED, et al: Computer-assisted static/dynamic renal imaging: A screening test for renovascular hypertension? *J Nucl Med* 20:11–17, 1979
5. Chervu LR, Blaufox MD: Renal radiopharmaceuticals—An update. *Sem Nucl Med* 12:224–245, 1982
6. Chiarini C, Esposti ED, Lusinno F, et al: Renal scintigraphy versus renal vein renin activity for identifying and treating renovascular hypertension. *Nephron* 32:8–13, 1982
7. Nally JV, Gross ML, Potvin WJ, et al: A comparison of 90 second ^{99m}Tc-DTPA renal scans and 30 minute ^{131}I-hippuran renograms in the assessment of renal artery stenosis. *Kidney Int* 23:173a, 1983
8. Fine EJ, Scharf SC, Blaufox DM: The role of nuclear medicine in evaluating the hypertensive patient. In *Nuclear Medicine Annual 1984*, Freeman LM and Weissman HS, eds. New York, Raven Press, 1984, pp 23–79
9. Sokal RR, Rohlf FJ: *Biometry*, San Francisco, W.H. Freeman and Company, 1969, pp 220–223
10. DeForrest JM, Davis JO, Freeman RH, et al: Separate renal function studies in conscious dogs with renovascular hypertension. *Am J Physiol* 235(4):F310–F316, 1978
11. MacKay A, Eadie AS, Cumming AMM, et al: Assessment of total and divided renal plasma flow by ^{123}I-hippuran renography. *Kidney Int* 19:49–57, 1981
12. Dubovsky EV, Russell CD: Quantitation of renal function with glomerular and tubular agents. *Sem Nucl Med* 12:308–328, 1982
13. Potvin WJ, Gross ML, Riccobono XJ, et al: A comparison of ^{99m}Tc-DTPA and ^{131}I-hippuran time activity curves in normal subjects. *Med Phys* 11:374, 1984
14. Nally JV, Clarke HS, Grecos GP, et al: ^{99m}Tc-DTPA flow studies with converting enzyme inhibition (CEI) in unilateral renal artery stenosis (uRAS). Proceedings of American Society of Nephrology, Washington, DC, 1984
15. Bender W, LaFrance N, Walker WG: Mechanism of deterioration in renal function in patients with renovascular hypertension treated with enalapril. *Hypertension* 6(Supp I):193–197, 1984
16. Oei HY, Geyskes GG, Mees EJD, et al: Captopril induced renographic alteration in unilateral renal artery stenosis. *J Nucl Med* 25:P36, 1984 (abstr)
17. Diffey BL, Hall FM, Corfield JR: The ^{99}Tc-DTPA dynamic renal scan with deconvolution analysis. *J Nucl Med* 17(5):352–355, 1976
18. Ying CY, Tifft CP, Gavras H, et al: Renal revascularization in the azotemic hypertensive patient resistant to therapy. *N Eng J Med* 311:1070–1075, 1984
19. Potvin WJ, Windham JP, Low LR, et al: Computer-simulated 90 second Tc^{99m}DTPA time-activity curve for use in assessment of renal artery stenosis. Proceedings of American Association of Physicists in Medicine, Seattle, WA, August 1985