# Imaging

## Comprehensive Renal Function Studies: Technical Aspects

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***A combined in vitro–in vivo renal function procedure has proved to be an important clinical tool in the nuclear medicine laboratory. This noninvasive test is relatively simple from the patient's standpoint. For the technologist, however, it involves scintigraphic imaging as well as a complex series of calculations including effective renal plasma flow, excretion rates, bladder retention, etc., all derived from a single injection of $^{131}$I-ortho-iodohippurate.***

A comprehensive nuclear medicine renal function study (CRFS) that combines renal scintigraphy, urine excretion rates, and effective renal plasma flow (ERPF) determinations *(1)* has been selected as a screening procedure to rule out functional disorders of the kidney by our urology department. The CRFS has proved to be a very sensitive test in the diagnosis of both bilateral and unilateral disease before it is evident by other tests and for following patients after surgery *(2)*. The same test assists in the evaluation of renal function of kidney donors and of grafted patients immediately after transplantation *(3)*. Complex testing of renal function is performed on an outpatient basis in all long-term transplants and urology clinic patients.

The purpose of this paper is to discuss the technological aspects of the performance of this procedure step by step.

### Method

From the patient's point of view, the test is relatively simple. He is injected with $^{131}$I-orthoiodohippurate (OIH) under a scintillation camera. The kidney areas are imaged continuously for 30 min. The bladder is then imaged. He voids. The bladder is reimaged. The blood sample is drawn 44 min after injection. He is dismissed.

From the technologist's point of view the test is more complex.

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**Radiopharmaceutical preparation:** After registration of each new lot of OIH, quality control procedures are carried out to ascertain that the radioactivity estimation by the manufacturer is accurate and that the material contains no free radioiodide. Checks of the injected dose aliquot against known samples in a well counter suffices for the former; paper chromatography by the method of Burbank *(4)* is used for the latter. It is imperative that doses containing less than 1.5% free iodide be used for renal function studies *(5)*.

Administered doses were as follows: 50 $\mu$Ci for patients under 1 year of age, 100 $\mu$Ci for 1-to 6-year-olds, 100 $\mu$Ci/kidney for 6- to 15-year-olds, and 150 $\mu$Ci/kidney for patients over 15.

**Hydration.** Urology and transplantation patients were routinely given 500 ml water to drink 30 min before the test to asure adequate urine flow. Patients investigated for renal vascular hypertension were studied in relative dehydration since this state intensifies the effects of the disease on the curves *(6)*.

Urine specific gravity is determined in order to monitor the degree of hydration. Although hydration shortens the mean transit time of OIH through the kidney, it does not basically effect the nature of this procedure.

**Positioning of patient.** Urology clinic patients were imaged in a supine position with the detector positioned posteriorly. Bladder counts were obtained with the camera detector positioned anteriorly to the patient. Whenever possible, this was achieved by having the patient assume a prone position rather than by repositioning the detector.

Renal transplant patients were imaged in a supine position with the detector positioned anteriorly over the pelvis with the bladder and transplanted kidney is in the full field of view.

The Ohio-Nuclear Series 110 wide field of view scintillation camera—combined with the Series 150 DataSystem, 100-11 Ultimat, and Informatek Simis 3 computer—was used to obtain these data.

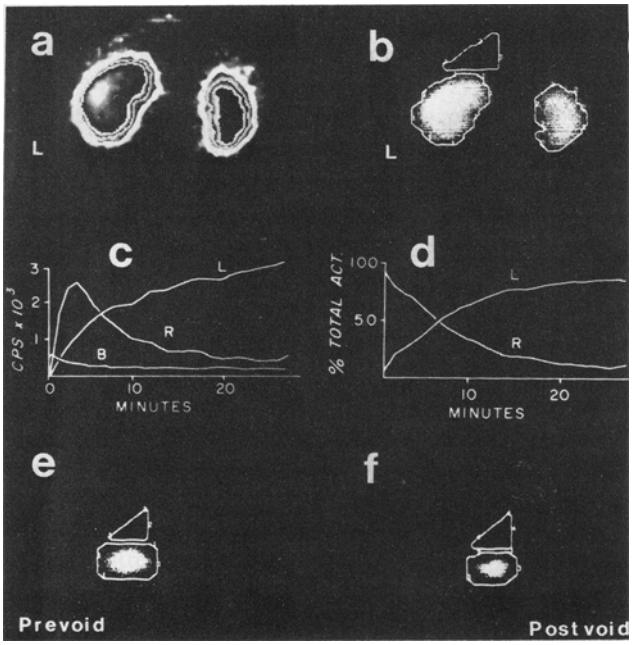


**FIG. 1.** Renographic images and curves after injecting $^{131}$I-orthoiodohippurate into patient with left pyelonephritis. Image (a) depicts all counts obtained over 27 min (usually represented in color). Lines are plotted by computer to form ROI. (b) Triangular area above left kidney is chosen for background. Area-corrected body background is subtracted from images and other curves: (c) right, left kidney, background; (d) right, left differential plots; and (e) (f) before and after voiding bladder images showing isointensity contours and background area selection.

## Data Collection

**Quantitative scintigraphy.** Throughout the study, the scintigraphic data were recorded on an Informatek Simis 3 computer. Kidney studies were recorded as a series of 27 frames in 64 × 64 matrices. Pre- and postvoid bladder images were then recorded, also in 64 × 64 matrix definition.

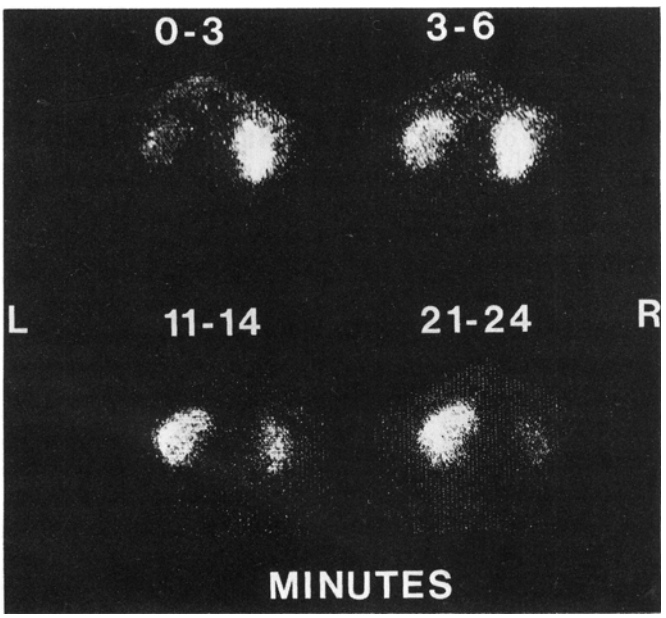


**FIG. 2.** Scintigrams made (a) 0-3, (b) 3-6, (c) 11-14, and (d) 21-24 min after injection of $^{131}$I-orthoiodohippurate. Right kidney is seen to decrease in activity sequentially and left to increase.

The full 27-min images were first added and isocontour plots were made over both kidneys and bladder for region of interest (ROI) selection (Fig. 1). An extrarenal area was delineated to serve as a representative background field. This was usually a triangular area above the left kidney about one-half to three-quarters the size of the kidney. Activity in this ROI was normalized to the area of each kidney, subtracted, and the images were redisplayed along with sequential net counts of each kidney and the background curves.

In order to calculate renal plasma flow of each kidney, each net renographic curve was then integrated up to the second minute. Right and left integrals were then expressed as percentages of the total counts. The resultant fractions were then multiplied by total ERPF to yield differential clearance rates. In the transplant, when one kidney and the bladder were visualized together, ROIs were chosen by "bug" or joystick, and net activity curves were plotted over each without calculation of differential rates.

In addition to the 27-min kidney plot, the computer displayed on a color television screen four other images taken at 0-3, 3-6, 11-14, and 21-24 min, color coded to maximum intensity (Fig. 2). These, along with the data shown in Fig. 1, were photographed for inclusion into the patient's record *(7)*.

**Standards and specimens preparation.** Using a 1-ml syringe, 0.6 ml OIH was removed aseptically from the vial and expelled into a small plastic tube. Using a volumetric pipette, 0.5 ml were transferred into a 50-ml volumetric flask which was then filled to the mark with tap water. This was designated stock solution and it was transferred into two 30-ml vials (1:100 dilution).

When a test was to be performed, an amount equal in volume to that injected into the patient was withdrawn from the stock solution, *using the same type of syringe and needle*, and added to a 100-ml volumetric flask filled to the mark with tap water. This was designated the working solution.

Two 2-ml working solutions, plasma, and diluted urine (1:100) were counted in an automatic well counter. The volume and specific activity of the urine were recorded.

**Calculation of ERPF.** ERPF may be calculated with great accuracy from the use of a single sample of plasma taken 44 min after injection, and the use of appropriate regression equations *(8)*. This takes the form of a polynomial,

$$y = a + bx + cx^2,$$

where y = ERPF; x = the dose injected (total counts/s ÷ counts/s per liter plasma; and a, b, and c are the coefficients −96.9, 10. 9, and −0.0454, respectively.

For example, if an injected dose aliquot yields 742.8 counts/s (1:10,000 dilution), and a plasma sample yields 77.7 net counts/s per ml (1:1000 dilution), then

$$x = \frac{742.8 \times 10{,}000}{77.7 \times 1000} = 95.6,$$

$$x^2 = 9139.1,$$

and ERPF = $-96.9 + (10.9 \times 95.6) + (-0.0454 \times 9139.1) =$ 530 ml/min.

**Normalization of ERPF.** Since ERPF varies linearly with body surface area (SA) *(9)* in nonobese adults, we related the individual ERPF value to the norm by the formula proposed by DuBois and DuBois *(10)*:

$$SA = 0.007184 \times ht^{0.725} \times wt^{0.425},$$

by normalizing all to a constant SA of 1.73 $m^2$. Adult *(11)* and pediatric *(12)* nomograms have been presented in the literature. We have found the mean uncorrected ERPF in normal subjects with two kidneys to be 525 ml/min ± 36, and 346 ml/min ± 83 for patients with one kidney. The surface-area corrected value was not used in other calculations. Its sole purpose was to determine whether the ERPFs obtained were within limits based on this correction or not.

**Calculation of predicted OIH excretion.** Among other factors, the amount of OIH excreted into the urine depends on renal plasma flow and on the time interval between injection and voiding. Regression equations for the prediction of the percentage injection dose expected in the urine at various times and at various ERPF levels have been developed. Since the values obtained at 35 min appeared to be most discriminating, we used the equation based on that sampling time: percent injected dose in urine at 35 min = $17.226 + (0.192 \times \text{ERPF}) + (-0.00015 \times \text{ERPF}^2)$. For example, at an ERPF of 530 ml/min, expected excretion = $17.226 + (0.192 \times 530) + (-0.00015 \times 530^2)$ = 77.6% injected dose.

**Calculation of actual OIH excretion.** The percentage of the injected dose excreted in the voided urine is calculated by the formula

$$\frac{\text{urine net counts/s} \times 100}{\text{standard net counts/s}}.$$

For example, an injected dose aliquot yields 742.8 counts/s (1:10,000 dilution) and urine yields 43.1 counts/s per ml (1:100 dilution). If the urine volume at 35 min is 76 ml, the actual OIH excretion is

$$\frac{431 \times 100 \times 76 \times 100}{742.8 \times 10000} = 44.1\%.$$

**Calculation of activity remaining in the bladder.** The percentage injected dose excreted by the kidneys, but remaining in the bladder, is calculated from the bladder net counts/s obtained from the scintillation camera before and after the patient voided (Fig. 1) and from the voided urine counts/s second and volume by the formula

$$\frac{\text{ml urine at 35} \times \text{postvoid net bladder counts/s}}{\text{prevoid net bladder counts/s - postvoid net bladder counts/s}}$$

For example, if urine volume = 76.0 ml, net prevoid counts/s = 156.0, and net postvoid counts/s = 4.9, the difference is 151.1 counts/s and

$$\text{residual urine} = \frac{4.9 \times 76.0}{151.1} = 2.5 \text{ ml}.$$

We defined an ROI around the bladder by isointensity line selection before and after the patient voided, along with a background ROI obtained on each frame. Counts/s in the latter ROI were normalized to the areas of the respective bladder images (Fig. 1).

Percent injected dose in residual bladder urine

$$= \frac{\text{percent dose in urine} \times \text{mls of residual urine}}{\text{mls of urine collected}}.$$

For example,

$$\frac{44.1 \times 2.5}{76.0} = 1.4\% \text{ injected dose.}$$

The total excreted injected dose fraction was the sum of voided and residual bladder urine; in this case, 44.1% + 1.4% = 45.5% injected dose.

**Calculation of excretion index (EI).** The percentage index is defined as the total percent of injected dose of voided urine expressed as a fraction of the expected. In this case, 45.5 ÷ 76.6 = 0.59%

**Final report format.** Thus, on a final report on this case, we printed the following to accompany the scintigraphic data exemplified by Figs. 1 and 2.

ERPF: 530 ml/min.
ERPF/1.73$M^2$ SA: 419 ml/min.
Expected excretion: 76.6% injected dose.
Actual excretion: 44.1%
Bladder: 1.4%.
Total: 45.5%.
EI: 0.60.
Residual bladder urine: 2.5 ml.

## Discussion

The CRFS should be generally applicable to all those departments with scintillation cameras equipped with divided crystal capabilities and a chart recorder attached to the output of each half. If computers are available, then body background subtraction, isointensity line ROI selection, and other aspects endowing greater precision can be effected. Virtually all of our developmental work was accomplished on systems without computers.

Under our present circumstances, technologist time for the data processing has been reduced to 20 min.

The advantage of this technique over other quantitative techniques is that comprehensive information can be gathered quickly, accurately, and reproducibly in a manner that can easily be accomplished by a nuclear medicine technologist and in a form that can be readily understood by the nuclear medicine physician.

We have found that the net renographic curves are es-

sentially identical in timing and intensity to those obtained by probe counting *(6)*. By integrating the first 2 min and determining the differential, we have found 2 min to be the best time to provide differential clearances at the degree of hydration we generally use. If the differential factor is computed for a time near the point of maximum activity or beyond, the integrals provide less accurate flow differential information.

The differential counting rate information as illustrated in Fig. 1(d) allows the physician to determine at a glance whether the two kidneys function in parallel fashion or not. In the example shown, it is clear that shortly after injection almost all the activity was in the right kidney, but that after 20 min almost all emanated from the left. Patterns for these and other data will be presented separately.

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