Routine Renal Scintigraphy with Sequential Injections of Technetium-99m-DTPA and Technetium-99m-MAG3

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Objective: To evaluate the use of sequential injections of ^{99m}Tc-diethylene-triaminepentaacetic acid (DTPA) and ^{99m}Tc-mercaptoacetyltriglycine (MAG3) for routine renal scintigraphy.

Method: Seventy-two sequential renograms were performed on 49 patients. After administration of 1 mCi of ^{99m}Tc-DTPA, data were collected for 7 min and 10 mCi of ^{99m}Tc-MAG3 were then injected. In 28 patients, furosemide was injected before ^{99m}Tc-MAG3. The time to reach peak activity, fractional renal function and retained cortical activity were calculated from the renogram curves. The total duration of the study was 30 min. The studies were analyzed by two independent observers. The GFR and ERPF were calculated using the RUPV method.

Results: There were six discrepant results for time to peak activity determination due to improper selection of the initial time (time = 0) or the peak activity. The discrepancies were corrected by setting the time = 0 to the first appearance of activity in the abdominal aorta above the kidneys and by selecting the last point in flat renogram curves or in curves with no distinguishable peak activity. The use of a diuretic prior to the administration of ^{99m}Tc-MAG3 resulted in further improvement of the interobserver agreement.

Conclusion: The sequential renogram is simple to perform, and provides excellent scintigraphic images and accurate functional evaluation of the kidneys using conventional gamma camera techniques.

Key Words: renal scintigraphy; technetium-99m-DTPA; technetium-99m-MAG3

J Nucl Med Technol 1994; 22:213–217

At our institution renal scintigraphy has been performed with simultaneous injections of ^{99m}Tc-diethylene-triaminepentaacetic acid (DTPA) and ^{131}I-hippuran (^{131}I-OIH) allowing a more complete evaluation of renal function and concurrent estimation of glomerular filtration rate (GFR) and effective renal plasma flow (ERPF).

The introduction of ^{99m}Tc-mercaptoacetyltriglycine (^{99m}Tc-MAG3), a technetium-labeled substitute for radiohippuran offering superior quality images and lower radiation dose to the patient (*1,2*), led us to re-evaluate our procedures for renal scintigraphy. This paper discusses the use of the sequential administrations of ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 for routine renography and for the calculation of GFR and ERPF.

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MATERIALS AND METHODS

This evaluation included 72 studies performed in 49 patients (31 females and 18 males; 31–81 yr in age) referred for the evaluation of hypertension.

All patients were studied supine with the gamma camera positioned underneath the imaging table. Data were collected at a rate of 1 frame every 15 sec for the 30-min study, using a Picker SX300 gamma camera interfaced to a PCS-512 computer (Picker International, Highland Heights, OH).

The patients were hydrated and instructed to void prior to the exam. Intravenous access was established in an antecubital or peripheral vein with tubing connected to a three-way stopcock.

After positioning, the patients were injected with a 0.5-ml bolus of 1.0 mCi of ^{99m}Tc-DTPA (MPI, DTPA Kit Chelate Multidose), followed by a 10-ml saline flush. This initial ^{99m}Tc-DTPA phase lasted 7 min and was followed by the administration of 10 mCi of ^{99m}Tc-MAG3 (Mallinkrodt, ^{99m}Tc Mertiatide) in 44 studies. In the other 28 patients, 40 mg of furosemide was administered by slow injection at the end of the ^{99m}Tc-DTPA phase prior to the injection of the second radiotracer. If the position of the patient had to be changed, it was done prior to the ^{99m}Tc-MAG3 injection. All these steps were performed without interrupting the computer collection.

During the procedure, in addition to the computer acquisition, two 3-min camera images were obtained of the ^{99m}Tc-DTPA phase. A dynamic study was imaged at one frame every 5 sec for 90 sec while injecting ^{99m}Tc-MAG3 and was followed by five static images at 5-min intervals. Two hours later, the kidneys were re-scanned for residual activity and the information stored in the computer.

Data Analysis

For quantitation purposes, the camera sensitivity was determined using 1 mCi of ^{99m}Tc-DTPA in a 10-ml saline-loaded syringe placed on the imaging table maintaining the

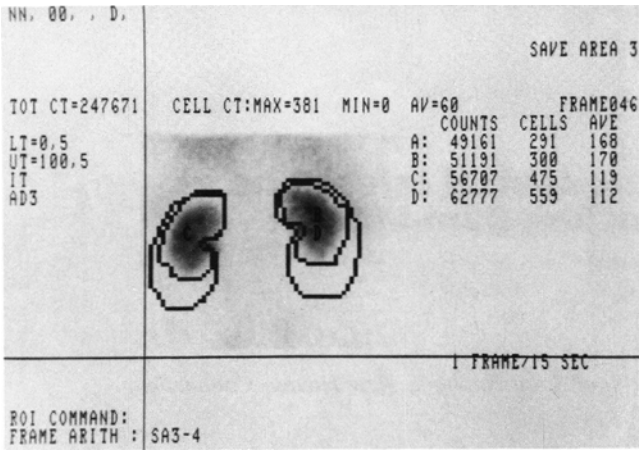


FIGURE 1. Regions of interest are drawn around each kidney. A second ROI is drawn to include the kidney and background. The background contribution is calculated by subtracting the renal activity from the larger ROI and after normalization for renal size is subtracted from the renal ROI.

same geometry as the patient study. This information was converted to counts per minute per microcurie.

The total injected doses, in microcuries, for ^{99m}Tc-DTPA and for ^{99m}Tc-MAG3 were calculated with a dose calibrator by measuring the activity before injection and then subtracting the activity remaining in the syringe after injection.

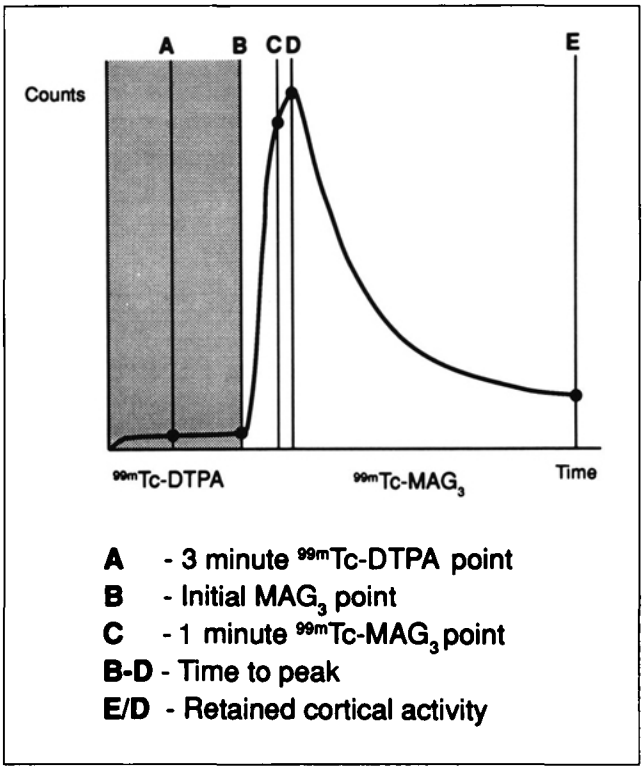


FIGURE 2. Time-activity curve obtained after the sequential injection of ^{99m}Tc-DTPA and ^{99m}Tc-MAG3. A point at 3 min after injection of ^{99m}Tc-DTPA (A) is selected for GFR calculation. The initial ^{99m}Tc-MAG3 point can be selected at the inflexion site (B) or over the abdominal aorta (see text).

These values are converted into total counts by multiplying the microcuries injected times the camera sensitivity expressed in counts per minute per microcurie.

The images were analyzed by drawing regions of interest (ROIs) over the left and right kidneys and concentric ROIs around both kidneys to correct for the contribution of background activity (Fig. 1). Another ROI was placed over the proximal abdominal aorta above the kidneys.

The background-corrected renogram showed an elevation of ^{99m}Tc-DTPA radioactivity during the first 10 min followed

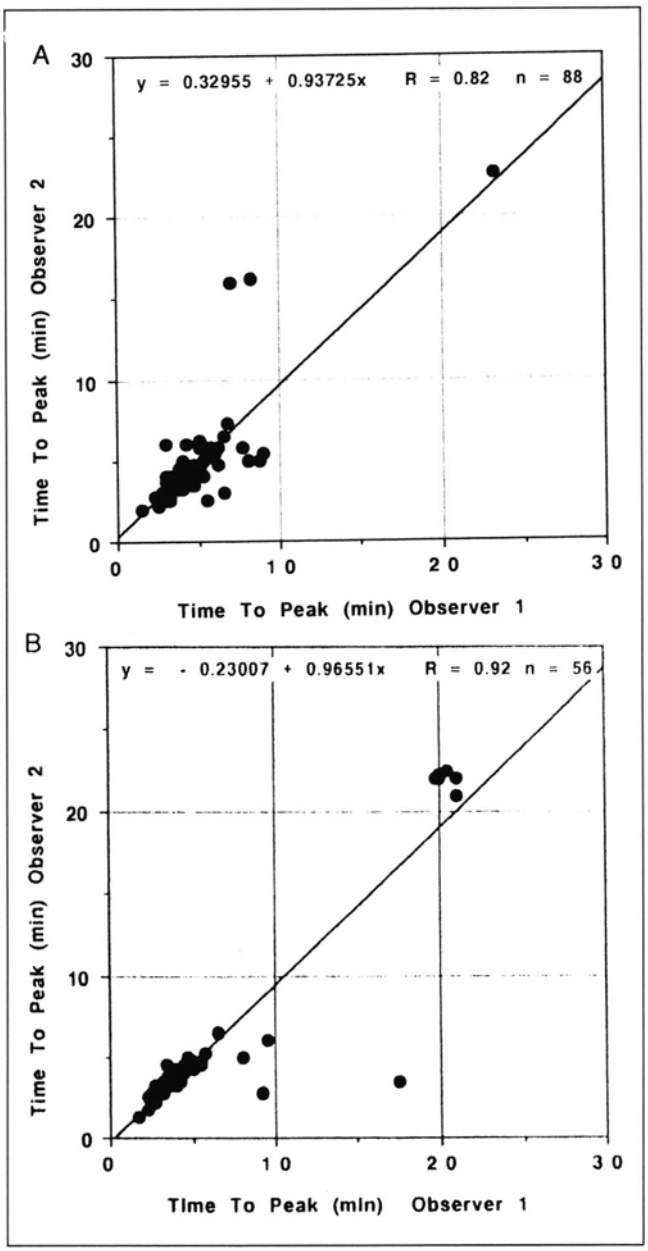


FIGURE 3. (A) Plot of the time to peak (min) for individual kidneys (n = 88), calculated by two independent observers. Studies performed without the administration of furosemide. (B) Plot of the time to peak activity (min) for individual kidneys (n = 56), calculated by two independent observers. Studies performed with the administration of furosemide.

by a sharp increase in activity corresponding to the ^{99m}Tc-MAG3 renogram section (Fig. 2). A point at 3-min into the ^{99m}Tc-DTPA curve was selected to calculate the GFR.

The time-activity plot for the abdominal aorta was displayed to select the point just before the sharp increase in ^{99m}Tc-MAG3 activity at the beginning of the renogram, i.e., zero time. The ^{99m}Tc-MAG3 renogram was then displayed and the time to peak activity, relative uptake for each kidney and retained cortical activity at 20 min expressed as the fraction of the maximum renal activity were calculated by selecting the peak activity point, a point 1 min into the study and the last point on the curve, respectively. The clearance of MAG3 (ERPF) was calculated using the point at 1 min in the renogram curve. The fractional activity can also be derived from these points.

We used the rate of renal uptake-plasma volume method (RUPV) to calculate the GFR (*3*) and ERPF (*4*). Briefly, the rate of renal uptake (U) was calculated from the cumulative renal activity at 3 min for GFR and at 1 min for ERPF and from the net injected activity. The plasma volume (PV) was calculated from the following equation (*5*):

$$PV = 84.5W^{0.80635}$$

where W is the patient's body weight in kilograms. The GFR (or ERPF) was then obtained from:

$$GFR(ERPF) = RU * PV$$

where RU is the rate of renal uptake, U/t, and t is the time over which the observation is carried out.

The tenfold increase in activity between the ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 injections make it unnecessary to correct for interference of the ^{99m}Tc-DTPA counts.

RESULTS

There were no discrepancies in the determination of fractional function and retained cortical activity.

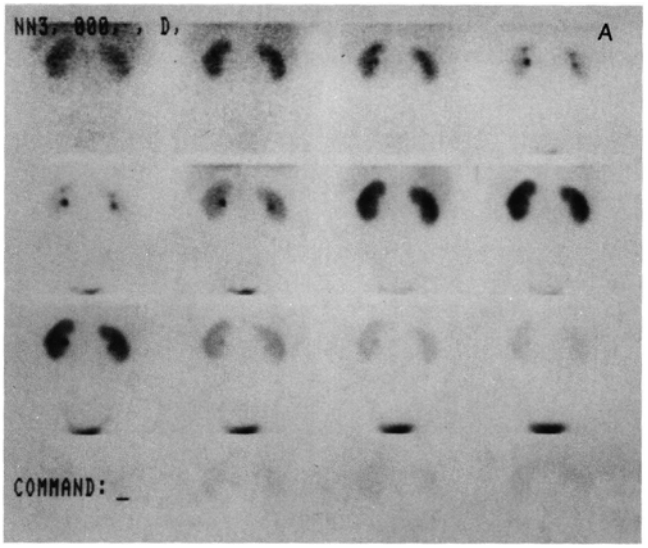
Figure 3 summarizes the results obtained independently by the two observers for the determination of the time to peak activity for each kidney. Significant discrepancies were seen in six cases. The reasons for disagreements included the wrong selection of the first point in the renogram curve in four cases, and in the other two cases, poor renal function that caused scattered points in the time-activity curves and continuous accumulation of activity without a discernible inflexion point identifiable as the peak activity. A repeat analysis using zero time as the data point preceding the first significant increase in counts from an ROI placed over the abdominal aorta, corrected the discrepancies in every case. When the discrepancy between the observers was due to the attempt to select a nonexistent renogram peak, selecting the last point in the curve solved the problem.

Patients who did not receive furosemide prior to the administration of ^{99m}Tc-MAG3 showed larger interobserver discrepancies than the furosemide-treated patients. The beneficial effect of furosemide is clearly shown by comparing the regression equation obtained in the nondiuretic group: $y = 0.33 + 0.94 \times$ ($r = 0.82$; $n = 88$) with the diuretic group: $y = 0.23 + 0.96 \times$ ($r = 0.92$; $n = 56$) (Fig. 3).

When the discrepancies were reanalyzed using the appropriate zero time and the last point on the renogram curves when there was poor renal function, the correlation coefficients were $r = 0.93$ for the nondiuretic group and $r = 0.99$ for the diuretic group.

DISCUSSION

The nuclear medicine practitioner has to decide on the best selection of techniques and radiotracers for the evalua-



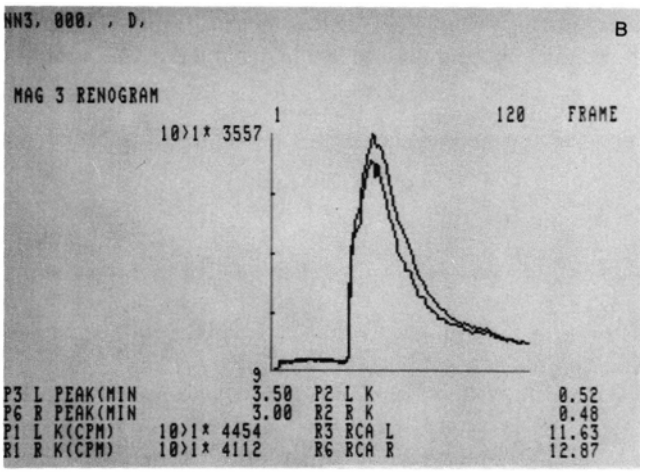


FIGURE 4. Normal ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 study. (A) The first six frames correspond to the ^{99m}Tc-DTPA phase. The ^{99m}Tc-MAG3 images show normal parenchymal and excretory phase. (B) Time-activity curves. The time to peak (P3, P6), fractional function (P2, R2) and retained cortical activity (R3, R6) are shown at the bottom of the curves. The counts at a selected time on the ^{99m}Tc-MAG3 curve are also shown (P1, R1).

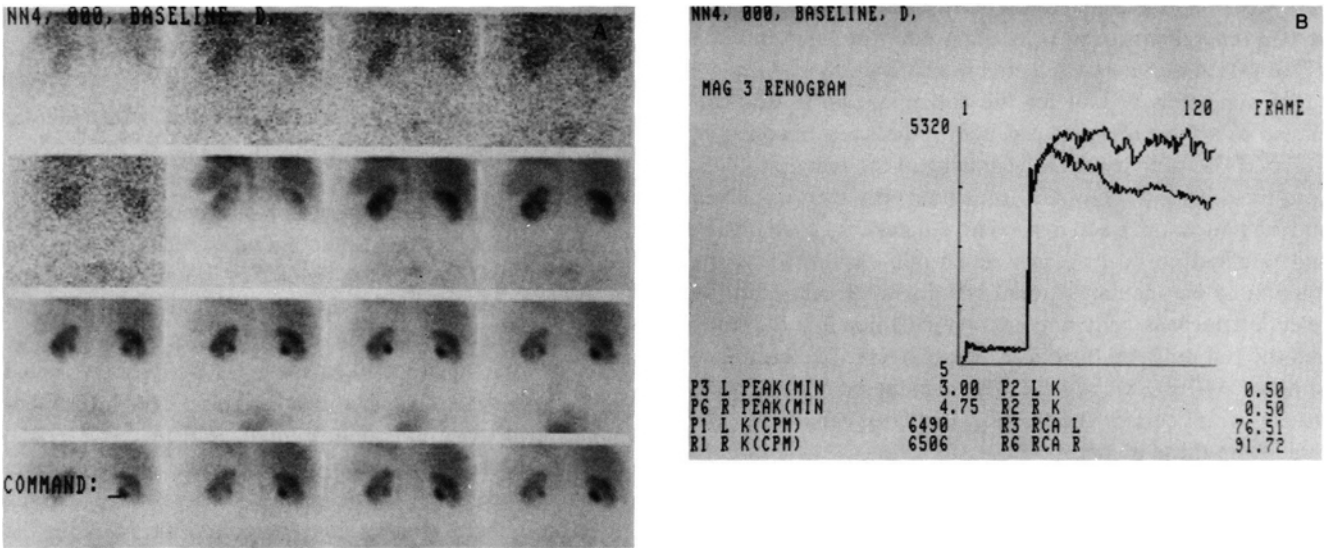


FIGURE 5. Chronic renal failure. (A) Adequate visualization of parenchymal and excretory phases in a patient with a creatinine of 5 mg/dl. (B) Renogram curves show symmetrical but abnormal patterns.

ation of renal function that maximizes the clinical information with minimal additional radiation exposure. This is particularly important at a time when the widespread adoption of gamma camera methods to calculate GFR and ERPF (*3,4,6–8*), the introduction of technetium-labeled pharmaceuticals similar to hippuran offering excellent images and lower radiation doses (*1,2,9*), as well as the successful use of renin-angiotensin-converting enzyme inhibitors renography (ACEI renogram) to evaluate renovascular hypertension (*10*) have increased the demand for radionuclide renography.

At our institution, it was customary to use ^{99m}Tc-DTPA and ^{131}I-OIH and differential spectrometry to obtain simultaneous renograms and to calculate the clearance of both agents. The use of ^{131}I-OIH is less than ideal because of the physical characteristics of ^{131}I which require medium-energy or high-energy collimators for imaging, the limitation in the total injected dose to 300 μCi and the need to administer Lugol's solution to reduce the radiation dose to the thyroid.

The blood clearance of ^{99m}Tc-MAG3 changes in direct relationship with hippuran clearance and hence with ERPF (*2*). The extraction of ^{99m}Tc-MAG3 is approximately three times greater than the extraction of ^{99m}Tc-DTPA, making ^{99m}Tc-MAG3 particularly valuable to study patients with poor renal function. Figures 4–6 show examples for various levels of renal function. The sequential use of ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 allows the simultaneous calculation of GFR and ERPF with 10 min of additional imaging time. Table 1 shows the combined total body radiation dose delivered by 1 mCi of ^{99m}Tc-DTPA and 10 mCi of ^{99m}Tc-MAG3 compared to the radiation received with the use of 10 mCi of ^{99m}Tc-DTPA and 300 μCi of ^{131}I-OIH.

The results highlighted a common and often neglected technical point in the calculation of the time to peak activity:

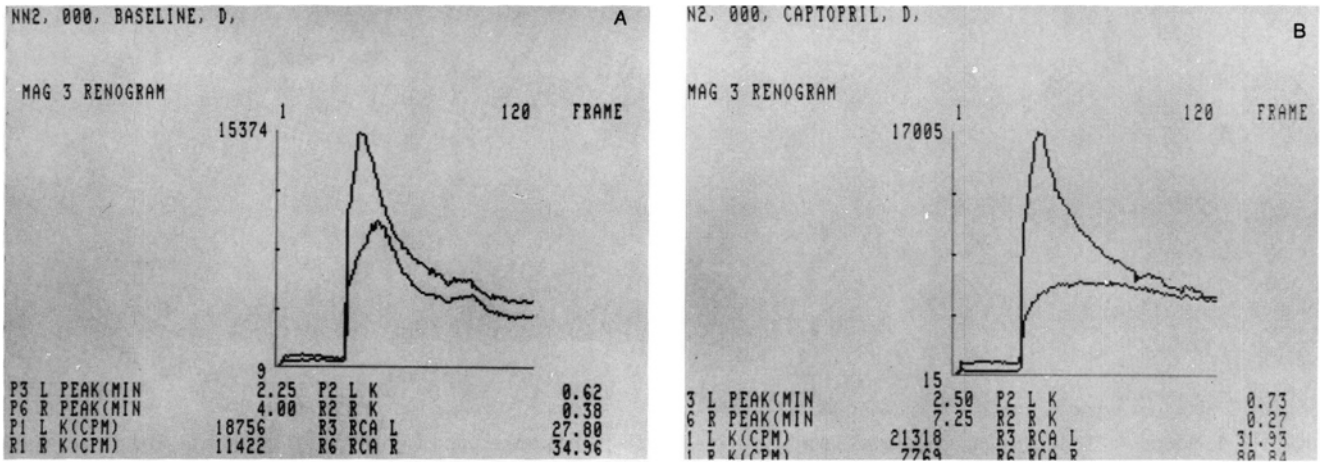


FIGURE 6. Renovascular hypertension. Baseline (A) and postcaptopril (B) renograms show characteristic changes of right kidney renin-angiotensin dependent function. The patient had a right renal stenosis.

TABLE 1
Radiation Doses for the Combined Use of Either ^{99m}Tc-DTPA and ^{99m}Tc-MAG3 or ^{99m}Tc-DTPA and ^{131}I-OIH

	DTPA/MAG3*	DTPA/OIH†
Whole-body	0.0587	0.137
Kidneys	0.164	0.31
Bladder wall‡	4.75	17.5

*Technetium-99m-DTPA: 1 mCi and ^{99m}Tc-MAG3: 10 mCi.
†Technetium-99m-DTPA: 10 mCi and ^{131}I-OIH: 300 μCi.
‡Bladder voiding interval = 4.8 hr.

the dependence on the proper selection of the zero time. Defining the zero time as the time of injection introduces uncertainties due to variations in the injection site, pre-renal circulation times and the actual recording of the time of injection. We define the zero time as the time at which there is a sudden rise in activity over the proximal abdominal aorta (Fig. 2, B). Thus, the time to peak activity derived from this internal reference point is independent of the factors mentioned above.

Variations in the shape of the renogram curves with poor definition of a peak activity resulted from the inclusion of the collecting system in the renal ROI. Careful use of the joystick in drawing the renal cortex regions or subtraction of the renal pelvis from the renal images before selection of the ROIs can minimize this source of error. We have excellent results in eliminating radiotracer from the renal pelvis using furosemide minutes before the injection of ^{99m}Tc-MAG3. The diuretic response cleared any residual activity from the calyces and renal pelvis in almost every case. This step is not needed for the DTPA part of the study since the information is obtained in the initial 3 min postinjection, before the tracer is in the collecting system.

Patient movement during the study, poor positioning or computer malfunction are problems common to all scintigraphic studies. The sequential method has the advantage to allow the repositioning of the patient before advancing to the main part of the study. In cases where this maneuver was needed, two separate sets of ROIs were required for analysis of the ^{99m}Tc-DTPA clearance calculation and of the ^{99m}Tc-MAG3 clearance and renogram.

The sequential renogram is easy to perform and the analysis of the renogram allows the calculation of both GFR and ERPF using a gamma camera technique. With proper technique, the interobserver variability for the calculation of these functional parameters is insignificant (*3,4*).

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