

# Dynamic Renal Scintigraphy

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## 1. Introduction

Patients referred for renography either have partial kidney obstruction or no obstruction. Partial obstruction is defined, as a level of resistance to outflow that if untreated will lead to loss of function. Complete obstruction rapidly leads to a non-functional kidney. For dynamic renal scanning a fast intravenous bolus of a radiopharmaceutical is injected. The radiopharmaceutical is rapidly excreted through the kidneys. This process is assessed by dynamic serial scintigraphy. Using a computer system, time-activity curves are constructed for both kidneys.

Some medication such as diuretics and angiotensin-converting enzyme inhibitors (ACE-inhibitors) have a specific influence on the processing of the radiopharmaceutical by the kidney. These drugs may be used depending on the information required by the clinician. Typically used radiopharmaceuticals are  $^{99m}\text{Tc}$ -DTPA,  $^{99m}\text{Tc}$ -MAG3 and  $^{123}\text{I}$ -OIH. DTPA is subject to glomerular filtration (extraction fraction  $\pm 20\%$ ), OIH is subject to both glomerular filtration and tubular excretion and MAG3 primarily undergoes tubular excretion (extraction fraction 40-50%). DTPA, as well as  $^{125}\text{I}$  Iothalamate and  $^{51}\text{C}$  EDTA, can be used to quantify the glomerular filtration rate (GFR).  $^{99m}\text{Tc}$  MAG3 is preferable to  $^{99m}\text{Tc}$  DTPA in patients with suspected obstruction and/or impaired renal function due to its more efficient extraction.

A first pass assessment for count statistics may be carried out immediately after a bolus injection of 370 MBq  $^{99m}\text{Tc}$ . This is only advisable if there is suspected acute tubular necrosis where dissociation occurs between the flow (which remains good) and the uptake (which is reduced) in transplanted kidneys.

Some centres determine the renal clearance from the plasma disappearance curve during dynamic renal scanning. Others calculate the renal clearance or renal function index from the renal uptake or activity in the kidney and bladder. This additional data is useful in renal transplant patients, for whom the investigation is often repeated (the patient is his own control).

PET provides high spatial resolution, high sensitivity, and quantitative accuracy. Several radiopharmaceuticals are available for functional renal imaging. However, they are currently limited to research applications.

## 2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## 3. Indications

- a. All uropathies which require evaluation of individual renal function at diagnosis, during different phases of surgical or conservative treatment or which require

evaluation of drainage function. Examples: follow-up of unilateral renal abnormality (reflux nephropathy, kidney stones, post pyeloplasty, renal artery stenosis), aiding the decision between nephrectomy or salvage operation of a diseased kidney, pre-assessment for kidney transplantation.

- b. Suspected urinary tract obstruction( use diuretic).
- c. Assessment of complications after a kidney transplant.
- d. Sudden reduction of renal function with no obvious cause.
- e. Detection of kidney damage after trauma or lithotripsy.
- f. Suspected renal vascular disease (use ACE inhibitor); however currently, the most appropriate diagnostic methods for this indication are CT angiography or MR angiography.

#### 4. Relation to other diagnostic procedures

- a. In suspected renovascular hypertension, CT and MR angiography are currently the preferred methods of investigation. These are more sensitive and specific for detecting renal artery stenosis than captopril-dynamic renal scanning is.
- b. Urinary tract obstruction can in principle be excluded, if the IVP or ultrasound is normal. A dilated system may complicate the assessment of obstructive disease, or even make the assessment impossible. Diuresis renography can confirm or exclude renal obstruction in 85% of suspected cases. In 15%, the diagnosis is only possible using the so-called Whitaker pressure-flow test. Diuresis renography also plays an important role in the diagnostic decision tree in neonates with a dilated renal pelvis.

#### 5. Medical information necessary for planning

The individual's past medical history, including anatomical abnormalities and surgery to the urinary tract, is essential for the interpretation of dynamic renography. There should be a clearly formulated clinical question/ query.

Furthermore, in order to carry out an optimal investigation, the serum creatinine level and the eGFR are required for an overall estimate of the renal function. It is also important to know whether the patient has a fluid restriction or uses diuretics or other drugs that may interfere with the test e.g. NSAID's. The drug history (particularly use of diuretics and ACE inhibitors) is essential if captopril is used as premedication in patients with hypertension.

#### 6. Radiopharmaceutical

Tracer	Nuclide	Doses (MBq)	Minimum doses (MBq)
<sup>99m</sup> Tc tiatide (MAG3)	Technetium-99m	70-100	15
<sup>99m</sup> Tc pentetate (DTPA)	Technetium-99m	150-200	20
<sup>123</sup> I-sodium iodohippurate (OIH)	Iodine-123	75	10

## 7. Radiation safety

### a. *Pregnancy*

Considering the relatively low dose, <100 MBq <sup>99m</sup>Tc MAG3, and the short biological half-life, the benefits of the diagnostic revenue quickly outweigh the assumed risk to the foetus. The external radiation dose received by the foetus, after intravenous administration of 75 MBq <sup>99m</sup>Tc MAG3 to the mother, is approximately 0,9 mGy. No foetal health detriment has been reported for doses <100 mGy. For <sup>99m</sup>Tc DTPA the dose to the unborn child is 1,6 mGy and for <sup>123</sup>I IOH this is 1,2 mGy.

### b. *Lactation*

According to ICRP 106 there is no need to interrupt breastfeeding after use of <sup>99m</sup>Tc MAG3 or <sup>99m</sup>Tc DTPA, but due to possible free <sup>99m</sup>Tc pertechnetate it is advisable to interrupt the feeding for 4 h. After the use of <sup>123</sup>I IOH breastfeeding should be interrupted for 12 h.

### c. *Radiation exposure*

A recent publication (ICRP 80) suggests lower radiation exposure is achieved with bladder voiding. The dose to the bladder wall contributes 80% of the effective dose. Frequent voiding after the study helps to reduce radiation exposure.

Due to the low dose, < 100 MBq <sup>99m</sup>Tc, and the bio-kinetics of the chemical carrier of <sup>99m</sup>Tc the effective dose to a healthy person is estimated at 0,02 mSv. For those with unilateral renal obstruction the dose will be approximately 0,75 mSv.

## 8. Patient preparation/essentials for procedure

- a. It is important to ensure ample diuresis during the investigation. Reduced diuresis due to poor hydration can lead to false positive results. Patients should drink 300-500 ml (5-10 ml/kg body weight), at least 30 min prior to the investigation. Glucose 5% i.v. may be used to hydrate infants who cannot drink enough (10 ml/kg body weight).
- b. Diuretics should be discontinued for 3 days prior to the investigation. Patients on diuretics produce less urine with the above mentioned fluid load and are at increased risk of a serious hypotensive response to captopril, which is used in the diagnosis of renal artery stenosis.
- c. MR and/or CT angiography are more appropriate methods of investigation for renal artery stenosis. However, renography can also be done in this case. The sensitivity and specificity of the dynamic renal scan is higher if captopril is administered. Administer 25 mg of captopril orally, 1 h before the scan. In order to ensure proper resorption, the patient should fast for 4 h. Contraindications to captopril should be mentioned on the request form. After administration of captopril, the blood pressure must be checked every 15-30 min for 1 h. Beware of hypotension, this may lead to an abnormal renography. Patients should be well hydrated (consider stopping diuretics for three days).  
A severe drop in blood pressure can be counteracted through an infusion of saline. ACE-inhibitors should be stopped a few days prior to the investigation. It is not known how long after stopping an ACE-inhibitor, the original sensitivity of the renin-angiotensin-aldosterone system for ACE-inhibition will return.
- d. Diclofenac has been shown to inhibit spontaneous ureteric contraction, prolong transit time and delay time to peak height of the renography curve. Other non-steroidal anti-inflammatory drugs (NSAID's) might have a similar effect. The effect is

greater with  $^{99m}\text{Tc}$  DTPA renography compared to  $^{99m}\text{Tc}$  MAG3 renography.

- e. In diagnosing urinary tract obstruction, diuresis should be stimulated using 0.5 mg intravenous furosemide per kg body weight (for children the maximum dose is 20 mg and for adults with normal renal function 40 mg). This can be given at different times during the procedure, before or after the administration of the radiopharmaceutical (e.g. F-15, F0, F+2, F+10, F+15 or F+20). The maximum effect of an intravenously injected diuretic is after 15 min.

According to the literature, administration of furosemide prior to the investigation is preferred, especially in patients with a dilated renal pelvis. In patients with impaired renal function (GFR), more furosemide should be given. Furosemide must be injected slowly (20-40 mg/min) to avoid neuritis of the acoustic nerve as a possible complication.

- f. In patients with a functioning kidney transplant, furosemide administration prior to the renography increases the reliability of the investigation.
- g. A full bladder can bring about a drainage obstruction. Therefore, shortly before the investigation and before continuing the investigation with intravenous furosemide, the bladder must be voided.
- h. A percutaneous nephrostomy catheter can be clamped depending on the clinical question. In patients with a neobladder and cutaneous drainage, catheterization may be required prior to the investigation to minimize reflux.

### 9. Acquisitions and processing

Energy:  $^{99m}\text{Tc}$ -setting, 140 keV

$^{123}\text{I}$ -setting, 159 keV

Window: 15-20%

Collimator: LEAP (or possibly LEHR if kidney function is good) with  $^{99m}\text{Tc}$  pharmaceutical

Computer: Dynamic images with frames of 10-20 sec for 20 min, matrix 128×128. Use zoom mode in infants and small children when the investigation is conducted with a large field of view gamma camera. Display dynamic images at 1-2 min intervals

Duration of the investigation: usually not longer than 20 min

#### *Important for processing:*

- a. An investigation of 20 min duration is usually sufficient. If indicated, late images (1-24 h) may be useful in the diagnosis of urinary tract obstruction. If furosemide is given after the radiopharmaceutical, the investigation must be extended by 15-20 min. If, at the end of the investigation, high retention of activity is observed in the renal pelvis and/or ureter, a post-micturition recording must be made. Depending on the clinical query, the investigation will take place with a closed or open nephrostomy drain or bladder catheter.
- b. Calibration source: for renal transplant investigations it is useful to quantify how much activity activity is taken up by the kidney. In that case, a calibration source of about 10 MBq must be made for measurement with the gamma camera.
- c. Positioning: Imaging is usually performed in supine position with the kidneys and, if possible, the bladder in the field of view. This minimizes renal depth differences and

movement. If obstruction due to nephroptosis is suspected, the investigation can be carried out in a seated position. The seated scan can be compared to a scan in supine position. When imaging a kidney transplant, the camera position is anterior. If there is a big difference in depth of the kidney relative to the gamma camera, a correction may be applied using lateral images or an echo. Using a dual-head camera system and the geometric mean to measure and calculate the left-to-right ratio also solves this problem.

- d. Computer processing: The relative function, an important item of information derived from the dynamic renal imaging investigation, is calculated by measuring the integral of counts in the renal ROI during 1-2; 1,5-2,5 or 2-3 min after injection. The normal function range is 45-55%. The relative function is strongly influenced by the size of the renal ROI and the position of the background ROI. In order to ensure reproducibility of the left-to-right ratio, these ROIs must always be chosen in the same manner. This can be achieved by having the ROIs determined by the computer according to a standardised method or by saving the selected ROIs, so that upon repetition of the investigation, identical ROIs can be selected. The image taken 1-4 min. after injection is well suited for contour detection. It is necessary, especially in children, to ensure the patient has not moved during the investigation. For calculating the left-to-right ratio, the literature describes different background ROIs: between the kidneys, below the kidneys, in a crescent shape around the kidneys, etc. The advantage of background between the kidneys is that it can always be well defined with a view to possible follow-up investigation. When using DTPA and MAG3, an overcorrection is obtained in the background between the kidneys because the tracer concentration in the blood is at a higher level. In renal impairment, the contribution of the liver activity is increased in the ROI of the right kidney. In the consensus report, a wedge-shaped background ROI around the kidney is recommended.
- e. In order to generate the time activity curve, the renal (whole kidney) ROI is used. If the objective is also to get an idea of the drainage from a dilated renal pelvis, then an extra ROI must be used. This can be done by measuring parenchymal function (transit time through cortex without interference of renal pelvis activity) using a cortex curve. Doubt has been cast upon the usefulness of the deconvolution technique.
- f. General Parameters:
  - Separate renal function, calculated from the renal uptake in the second minute, expressed in % of uptake in both kidneys together.
  - Time to peak (Tmax.), normal <5 min.
  - Half-time from Tmax, normal 15 min after tracer injection.
 Retention in calyces/pelvis can lead to prolonged half-time values.
- g. Parameters in kidney transplantation:
  - The uptake during the first 2 min and the first 10 min expressed as a percentage of the administered dose.
  - Excretion parameters: tubular transit index and excretion index.

## 10. Interpretation

- a. Quality check; e.g. extravasation, bolus technique, patient position, movement, acquisition starting time and whether there is already excretion of activity in the renal

- pelvis at time of relative function measuring.
- b. In a unilateral supra-vesical urinary tract obstruction, the obstructed kidney is usually larger than the normal contralateral kidney and displays a dilated renal pelvis. This dilated system is initially displayed as a cold area that is later filled with activity. Excretion into the system is delayed (>5 min) after which there is retention in the renal pelvis and the ureter above the obstruction. Usually this excretion takes place during the investigation, but in severe obstruction this can only be seen on the late images, made 1-24 h after injection. If the excretion into the renal pelvis takes place within 5 min, a serious obstruction can be excluded. Compared to the contralateral kidney, the overall cortical uptake is lower and the curve shows a prolonged time to peak as well as a delayed excretory phase. If there is poor renal function, scintigraphy and time activity curves are harder to interpret, partly because of a decreased response to furosemide. Bilateral supra-vesical obstruction is rare; a two-sided expansion of the urinary drainage system generally occurs due to an infra-vesical obstruction or bladder emptying disorder of other causation. In this group of patients, an obstructive picture can be observed as a consequence of increased hydrostatic pressure in the bladder. In this case the investigation may need to be carried out with an open urinary catheter. The probability of an anatomical obstruction is low if the retention in the renal pelvis and/or ureter disappears after micturition. With F-15 or FO a  $T_{1/2}$  greater than 20 min is compatible with obstruction.
  - c. Unilateral renal artery stenosis usually results in a smaller kidney as compared to the contralateral side. The affected kidney shows delayed excretion into the renal pelvis and the curve shows a longer time to peak (Tmax.) than that of the contralateral kidney. When using OIH or MAG3, more severe stenosis result in a curve that does not decrease and retention in the parenchyma will be apparent on the scintigram. With DTPA, however, only the peak of the first passage can be observed, after which the dynamic renal scan shows no uptake or secretory phase in severe stenosis; the scintigram shows a vague image of the affected kidney. The sensitivity of this investigation is increased through provocation with captopril: a deterioration of the excretory phase occurs as observed in severe stenosis, even in those cases which initially show symmetrical excretion. If the affected kidney shows excretion to the renal pelvis within one minute of the healthy kidney, then unilateral renal artery stenosis is unlikely. The use of captopril also increases the sensitivity of the diagnosis in bilateral renal artery stenosis. Captopril can bring about a severe drop in blood pressure, +/- collapse, due to a vasovagal reaction in patients with bilateral renal artery stenosis. In this situation the serial scintigram shows parenchymal retention in both kidneys.
  - d. In acute renal insufficiency, such as acute tubular necrosis or after administration of a large amount of contrast medium for angiography, the scintigram also shows bilateral parenchymal retention and the kidney curves show a rising or flat course throughout the entire investigation. In patients with acute renal insufficiency, a (relatively) normal MAG3 or OIH scintigram argues in favour of improving renal function in the future; of course, the prognosis depends on the reversibility of the underlying cause.
  - e. In renal transplantation, renography is complementary to sonography, which is usually the first investigation to evaluate renal graft dysfunction. This method can detect acute rejection as well as urological complications, e.g. urinary tract

obstruction, urine leakage or other complications leading to irreversible damage of the graft. Classically acute tubular necrosis presents with relatively good perfusion accompanied by delayed uptake and excretion. Rejection presents as diminished flow with delayed uptake and excretion. Escape of activity from the urinary tract indicates a urinary leakage. Sometimes it is difficult to recognise this. Uptake after micturition/ catheterisation and comparison with previous investigations may facilitate the interpretation. If there is leakage, the beginning of excretion is usually not delayed. Serial measurements of OIH or MAG3 uptake by the transplanted kidney, may allow detection of acute rejection even before biochemical abnormalities occur or in a period of oligo-anuria. Acute rejection also causes delayed excretion in an already functioning transplant. Abnormalities, on a renal scan, that are due to acute rejection are similar to those of cyclosporin nephrotoxicity.

- f. Although the literature lists reference values of renography parameters, visual interpretation will often suffice. The time to peak (Tmax) and the decrease in the excretory phase are strongly influenced by diuresis during the investigation. When diuresis is low, the time to peak may be unilaterally extended and the decrease of the excretory phase may be delayed as in unilateral renal artery stenosis. However, on the serial scintigram, the excretion to the renal pelvis takes place simultaneously and within the normal amount of time (<5 min). A unilateral reduction in uptake is also seen in unilateral renal disease such as pyelonephritis. As described above, the serial scintigram plays an important role in the interpretation. Moreover, it enables anomalies of shape and ectopic location to be recognised. Cysts, tumours and infarcts are displayed as defects and are best identified at the start of the investigation. In infants and small children, one often visualises the stomach as a photon-deficient area above the left kidney. Scintigraphy obtained with <sup>99m</sup>Tc MAG3 has a higher contrast than with-DTPA as well as a higher resolution than <sup>123</sup>I-OIH. Nevertheless, cysts smaller than 3 cm are difficult to recognise.

## 11. Report

Clinical history, including symptoms and/or diagnosis, referral reason.

General information: procedure, date, activity, radiopharmaceutical, route of administration, previous studies for comparison, dosage and time of administration of diuretic or ACE-inhibitor, hydration prior to investigation.

*Findings:*

- Shape, size, location and overall symmetry of the kidneys.
- Homogeneity/ defects in activity in the kidneys.
- Whether the kidneys are symmetrical in activity accumulation.
- Time of excretion into the renal pelvis, ureter and bladder.
- Any retention of activity in the parenchyma, calyces, renal pelvis and/or ureter.
- Changes in post-micturition images .
- Any activity outside the urinary tract.
- The shape of the resulting time-activity curve.
- The split renal function percentages.
- Comparison to previous studies.

*Interpretation/conclusion:* address the reason of referral.

## 12. Literature

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