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GUIDELINES

Guidelines for standard and diuretic renogram in children

Isky Gordon · Amy Piepsz · Rune Sixt

Abstract Special consideration needs to be given to children who undergo dynamic renography. The Paediatric Committee of the European Association of Nuclear Medicine has updated the previous guidelines. Details are provided on how to manage the child, the equipment, and the acquisition and processing protocols. The pitfalls, difficulties and controversies that are encountered are also discussed, as well as the interpretation of the results.

Keywords Children · Renography · Diuretic · Obstruction

Disclaimer

This guideline summarises the views of the Paediatric Committee of the European Association of Nuclear Medicine (EANM) and reflects recommendations for which the EANM cannot be held responsible. These recommendations should be taken in the context of "good practice" of nuclear medicine and do not substitute for national and international legal or regulatory provisions. This guideline has been brought to the attention of the National Societies of Nuclear Medicine.

The guidelines have been reviewed by the EANM Dosimetry Committee, the EANM Physics Committee and the EANM Radiopharmacy Committee.

Purpose

The purpose of this guideline is to offer to the nuclear medicine team a framework, which could prove helpful in daily practice. This guideline contains information related to the acquisition, processing, interpretation and indications for standard renography in children. The present document is inspired by the desire of EANM and the American Society of Nuclear Medicine to have guidelines for most nuclear medicine procedures [1–4]. Part of this guideline has been strongly influenced by the consensus report on quality control of quantitative measurements of renal function published by the International Scientific Committee of Radionuclides in Nephrourology, following the meeting in Copenhagen, May 1998 [4], which also reflects the European practice.

Standard renography has been in use for some time; whilst there are variations in many aspects of renography, agreement has been reached about certain aspects. The consensus document from the International Scientific Committee of Radionuclides in Nephrourology has made various recommendations relating to estimation of differential renal function (DRF). Where evidence existed, that was used; otherwise the consensus document represents the considered opinion of a body of experts, based on their long experience and published as well as unpublished data. However, at times there are few data to support certain opinions and practices currently in use.

Under the Auspices of the Paediatric Committee of the European Association of Nuclear Medicine (chair: D. De Palma, Varese, Italy)

I. Gordon (✉)
Institute of Child Health,
London, UK
e-mail: I.Gordon@ich.ucl.ac.uk

A. Piepsz
CHU St Pierre,
Brussels, Belgium
e-mail: amypiepsz@yahoo.com

R. Sixt
The Queen Silvia Children's Hospital,
Göteborg, Sweden
e-mail: rune.sixt@mbox330.tele2.se

Background information and definition

Standard renography allows estimation of two aspects of renal function.

The first aspect is renal clearance, i.e. the extraction of a tracer from the blood. In this guideline only estimation of relative clearance, or DRF, will be discussed. The Paediatric Committee believes that there are important errors attached to the estimation of absolute clearance using only the gamma camera and therefore recommends a plasma clearance technique based on blood sampling for this purpose.

DRF estimation is best undertaken approximately between 1 and 2 min after tracer injection [4]: after 2 min, there is a possibility that some tracer has left the renal space, therefore invalidating the DRF estimation. The information obtained during this 1- to 2-min interval still, however, contains non-renal activity (background), which should be corrected. The tissue component and part of the vascular component can be removed by subtracting some activity around the kidney (see "Processing" section); the remaining part of the vascular component may be eliminated by introducing the Patlak-Rutland correction [5]. Controversy exists as to whether one or both corrections should be applied. Both corrections might be more relevant when tracers with low extraction rate such as diethylenetriamine-pentaacetic acid (DTPA) are used. Background correction is particularly important in estimation of DRF when there is asymmetrical renal function or decreased overall function.

The second function which can be assessed by renography is the excretion, or disappearance of the tracer from the kidney. This disappearance can simply be estimated by inspecting the renogram curve: an early peak followed by a rapidly descending phase is typical for normal excretion. A delay in excretion is characterised by a continuously ascending curve over 20 min or a curve that fails to fall and appears as a plateau. Several techniques have been proposed for quantifying the transit of tracer through the kidney. A comprehensive overview of the available methods can be found in a recent consensus paper [6]. These range from simple descriptive parameters, such as the time to reach the maximum of the curve, i.e. T_{max}, to more sophisticated parameters, such as deconvolution analysis, output efficiency (OE)/pelvic excretion efficiency (PEE) or normalised residual activity (NORA). Sufficient information is provided by the shape of the renogram and the T_{max} to discriminate between normal transit (T_{max} around 3 min) and very delayed transit (T_{max} of 20 min). When dilatation of the collecting system exists, the standard renogram is generally characterised by a continuously rising curve, reflecting poor drainage of the kidney. In this condition, furosemide should be administered which increases urinary flow and may distinguish between good, intermediary and poor drainage.

Controversy exists in four areas; these are hydration of the child, bladder status/bladder catheterisation, assessment of drainage post furosemide and the interpretation of impaired drainage [7].

Hydration of the child

The child should be adequately hydrated for both the standard and diuretic renogram. Infants could receive an additional bottle/breast feed while older children could be encouraged to drink liberally water/orange juice. The volume will be dependent on the child's size. Almost all children undergoing diuretic renography are outpatients and following the above recommendations they are neither salt nor water depleted at the time of the renogram. It is almost impossible to get every child into the same state of hydration even using intravenous hydration. The maximum effect of an intravenous diuretic is around 15 min after administration [8]. In the presence of hydronephrosis, when a diuretic renogram using a tubular agent is undertaken, the late post micturition (PM) images images are acquired 50–60 min after tracer injection. Independently of the timing of the diuretic injection (F −15; F 0 or F +2 or F +20) the diuretic has had a prolonged action by the time of the PM image. This means that maximum urine flow has been achieved before the acquisition of the PM data in all cases. So even if hydration was not ideal when starting the procedure, the administration of furosemide and the late PM images will result in a very good or complete drainage of a normal kidney [9]. Thus oral hydration prior to the diuretic renogram is considered adequate. In case of unilateral hydronephrosis, the child is adequately hydrated if the tracer is seen in the bladder by 10 min or earlier. If there is no tracer in the bladder at 20 min, then the child was dehydrated and caution should be exerted about the interpretation of drainage from either kidney unless there is a diuretic challenge and a late PM data set.

Bladder status and effect of gravity

In the presence of a full bladder, drainage from the kidney may be delayed, even in the normal kidney resulting in a flat renal curve. Young children cannot be expected to void immediately prior to the renogram; however, the use of a diuretic usually causes the child to void, often within 15–20 min of the administration of the diuretic. Additional data should be routinely acquired after micturition so that analysis of the kidneys can be undertaken when the bladder is empty. A further important aspect of this approach is to move the child to erect position some time after the administration of the diuretic to allow gravity to have its

effect and further reduce apparent poor renal drainage simply due to a dilated system in the supine position. As there is a significant time gap before the acquisition of the PM images, the infant or child should be erect for all or most of this period.

If the drainage after the standard renogram (0–20 min) is moderate and there are previous data to suggest that this is not due to obstruction, then some institutions undertake PM images first. If the drainage is still poor then furosemide may still be given followed by a second set of PM images. The routine acquisition of PM images has shown that bladder catheterisation is not required and is rarely if ever undertaken in most European nuclear medicine departments. In rare cases (e.g. neurogenic bladder) placing a catheter is advisable, but this can be postponed until the end of the furosemide test and following PM images if spontaneous bladder emptying does not occur.

Assessment of drainage post furosemide

Assessment of drainage has been radically changed over the past 15 or so years. The shape of the washout curve has been proposed to assess drainage [4]. The classic method of analysis of the post diuretic curve is to assess the slope of this curve; however, the determination of this slope is not straightforward and many variants have been proposed, each resulting in a different slope value [7]. In the presence of dilatation, analysis of the post furosemide curve on its own is inadequate since it assumes that all kidneys have the same function, secondly that all renal pelves have the same capacity, thirdly no attention is paid to whether the bladder is full or empty and finally gravity is not allowed to have its natural effect (see "Diuretic response" section and "Future perspectives" section). The PM images will take into account the variables of bladder status and the effect of gravity. There are no nuclear medicine techniques which take into account the volume of the renal pelvis (see "Future perspectives" section).

Interpretation of impaired drainage

The qualitative approach is nevertheless valid in some circumstances. A basic renogram curve showing a short time to maximum (T_{max}) followed by a descending curve and ending up with almost complete renal emptying excludes any significant impairment of drainage. This is also true with poor renal emptying at the end of the basic renogram followed by prompt and complete renal washout after administration of furosemide. A renogram with poor emptying during the basic renogram and following furosemide, but complete emptying on the late PM image, also excludes any significant impairment of drainage. Once good drainage has been achieved at any point in the diuretic renogram, then obstruction has been excluded and the risk to the kidney is small.

Alternatively, a continuously rising curve, even after furosemide, and a PM view demonstrating the presence of the same or more renal activity than at the end of furosemide test will lead to the conclusion of a poor drainage.

Unfortunately, these situations are generally not so clear. The simultaneous administration of furosemide and tracer (F 0 test) often produces, on the hydronephrotic side, a rather short T_{max}, followed by a horizontal renogram, which is difficult to interpret in terms of renal output. On the other hand, a reduced renal function will result, whatever the moment of diuretic injection, in reduced extraction of tracer from the blood and thus a slow filling of the dilated collecting renal pelvis and so very low unilateral function will often result in a wrong interpretation of poor drainage. In both cases, a quantitative approach offers a better estimation of the real washout.

Output efficiency and normalised residual activity

The definition, calculation and validation of these two parameters can be found in the recent literature [20–22].

Briefly, OE is the amount of tracer which has left the kidney at time t in per cent of what the kidney has taken up from the blood, while NORA is the remaining activity in the kidney at time t (over a period of 1 min) expressed as the ratio between time t and time 1–2 min. These parameters can be calculated at any point of the renogram. As the PM values take almost all the variables of drainage into account and is done at a constant time point after the injection of tracer, so this result offers the best possible assessment of drainage within a reasonable time period. If however the drainage is good after F 0 or F +20 renogram, then there is no need for PM views and one can determine OE and NORA at the end of the renogram in order to have a quantitative parameter to compare with at the next exam.

The advantage of these parameters is that they provide an estimation of the washout of a kidney, independently from the differential function of that kidney. OE has the advantage to be more independent of overall function than NORA, but programming of NORA within a renal software package is much easier, in particular for the PM data.

Quality controls

Adequate background correction is mandatory for both parameters [19–33]. For the calculation of NORA, one should define exactly the 1–2 min counts, the first frame corresponding to the peak of the heart curve. For OE, the integral of the heart curve has to be adapted to the initial part of the renogram. A visual representation of this

procedure may help to increase the robustness of the obtained number.

Main pitfalls in interpretation of whole kidney washout

As mention before, continuous increase of renal activity, even after furosemide and PM acquisition, should lead to the conclusion of poor washout. Causes of poor washout include a very dilated renal collecting system, as well as the immature or the poorly functioning kidney [23, 24]. Unfortunately, poor washout does not necessarily mean low urinary flow through a narrow segment.

It is therefore not recommended to conclude in the final report that the kidney is obstructed, simply because one is dealing with poor emptying of a dilated renal pelvis.

Radiopharmaceuticals used

There are three tracers that rely on tubular extraction, ^{123}I-hippuran, ^{99m}Tc-mercaptoacetyltriglycine (^{99m}Tc-MAG3) and ^{99m}Tc-ethylenedicysteine (^{99m}Tc-EC) and one tracer dependent on glomerular filtration, ^{99m}Tc-DTPA. The tracers reflecting tubular extraction have a greater renal extraction than ^{99m}Tc-DTPA, resulting in a lower background activity and a higher kidney to background ratio. For these reasons, the tubular agents are preferred to ^{99m}Tc-DTPA for estimation of DRF particularly in infants, for diuretic renography and indirect cystography. ^{99m}Tc-DTPA may be useful following renal transplantation when both blood flow as well as formal glomerular filtration rate (GFR) estimation (with blood sample analysis) is required.

The kidney of the young infant is immature and the renal clearance, even corrected for body surface, progressively increases until approximately 2 years of age. Therefore, renal uptake of tracer is particularly low in infants, with a high background activity. In young children, preference must be given to tracers with high extraction rate, such as ^{123}I-hippuran, ^{99m}Tc-MAG3 or ^{99m}Tc-EC. These tracers provide reasonable images and the DRF can already be estimated at the end of the first week of life. With ^{99m}Tc-DTPA, estimation of DRF may be inaccurate in early infancy. Once the infant has undergone the first renogram using ^{123}I-hippuran or ^{99m}Tc-MAG3, then all follow-up renograms should use the same tracer.

Indications/contraindications

Indications

A. All uropathies, which require evaluation of individual renal function at diagnosis and during the different phases of surgical or conservative treatment and evaluation of the drainage function. Examples include dilatation immaterial of the cause (e.g. pelvi-ureteric and vesico-ureteric stenosis), bladder dysfunction, complicated duplex kidney, post trauma, asymmetrical renal function and reflux nephropathy.
B. When dilatation of the collecting system exists, the standard renogram should be complemented by a diuretic renogram.
C. Preceding indirect radionuclide cystography (IRC).
D. Evaluation of sustained systemic hypertension. If renovascular disease is suspected then angiotensin-converting enzyme (ACE) inhibitor provocation may be used [3].
E. Renal trauma.
F. Follow-up of renal transplantation. Here the activity of tracer may be increased and a rapid acquisition is required (full details are not within the scope of this guideline) [10].

Contraindications

There are no contraindications. However, there are limitations: in the presence of poor renal function, accurate estimation of DRF and/or drainage may not be possible. In the presence of marked hydronephrosis, the interpretation of poor drainage is difficult since this could be due to either "partial hold-up" or simply because of the reservoir effect of the dilated system. In the presence of calculus obstruction, a renogram may be undertaken but no furosemide should be administered.

Procedure

Information about previous examinations relevant to this procedure

The clinical history, ultrasound data and previous radionuclide imaging should be reviewed. This may help the decision whether a standard renogram, a renogram followed by an indirect radionuclide cystogram or a diuretic renogram should be performed.

Patient preparation

Information with appointment letter

The parent/child should receive detailed written information, which explains the entire procedure. The parents should be told to offer the child drinks liberally before getting to the department. This is especially important in

hot weather [11–14]. When furosemide has been given, the parent should be warned that the child, who is toilet trained, may have an urgent need to void on more than one occasion following the procedure. Very seldom, the older child may suffer loin pain if a diuretic has been used.

Prior to injection

Hydration: the child should be encouraged to drink from the time of arrival in the department to the actual injection of tracer. The child (if co-operative) should be encouraged to void prior to the injection [11–14].

Anaesthetic cream: can be applied to relieve the discomfort of the injection, this requires a 60-min wait for the cream to have its effect and so provides an opportune time for ensuring good hydration.

If ^{123}I-hippuran is used, the thyroid should be blocked using perchlorate given 60 min before the tracer.

This guideline does not support the routine use of a bladder catheter.

Precautions

Be aware of orthostatic hypotension after furosemide injection.

Radiopharmaceutical

Radionuclide

Technetium-99m (^{99m}Tc), (Iodine-123 (^{123}I) for hippuran only).

Pharmaceutical

Tubular agents are recommended, such as MAG3, EC and hippuran.

If unavailable, DTPA may be used.

Dosage

Minimum activities recommended by the EANM are:

^{99m}Tc-MAG3=15 MBq
^{99m}Tc-DTPA=20 MBq
^{123}I-hippuran=10 MBq

Recommended maximum activities, corresponding to a 70-kg adult, are:

^{99m}Tc-MAG3=70 MBq
^{99m}Tc-DTPA=200 MBq
^{123}I-hippuran=75 MBq

Administered activities should be preferably scaled according to the new EANM paediatric dosage calculator [15].

Injection technique

Position the patient supine, start the acquisition and then inject the radiopharmaceutical as a bolus.

Radiation burden

A recent publication (ICRP 80) suggests the radiation exposure to be lower than that proposed in ICRP 62 because bladder voiding was not taken into account. As the dose to the bladder wall contributes 80% to the effective dose for these agents, frequent voiding after the study helps to reduce radiation exposure.

For a 5-year-old using ^{99m}Tc-DTPA the effective dose (ED) is 0.54–0.82 mSv, the lower figure relating to a 1-h voiding interval.

For ^{99m}Tc-MAG3 the corresponding figures are 0.20 and 0.38 mSv, respectively [16, 17], and for^{123}I-hippuran 0.41 and 0.7 mSv, respectively.

^{99m}Tc-DTPA and ^{123}I-hippuran require a reduction of the injected activity if the renal function is impaired [15].

Image acquisition

Zoom at acquisition

A zoomed acquisition makes it easier to draw the regions of interest (ROI) especially critical when there is gross hydronephrosis and the kidney extends laterally almost to the outer edge of the body. The ideal field of view includes the heart at the top and the suprapubic area at the bottom of the field of view. Poor positioning with for example excluding part of the kidney renders the study useless. This can easily be avoided by checking the position by means of a radioactive marker. Each department should calibrate the zoom in function of the child's body weight and the characteristics of the gamma camera. It is strongly recommended to use the same zoom for the three successive acquisitions (basic renogram, furosemide challenge, late PM images).

Dual-head gamma camera

This is not a recommended procedure in routine renography in children. In general, the posterior view offers the same information as the geometric mean [36, 37]. A main

drawback of this technique is that the child is placed in a sandwich between the two heads and this might create anxiety and child's motion. A possible application of the geometric mean with dynamic renography could be the ectopic kidney, which is always shifted in anterior position.

Intravenous injection of the tracer

There are two possible options depending on the experience of the person responsible for the injection. Either placing an intravenous line (Venflon) or injecting the tracer directly through a fine butterfly needle (size 27 or 25). The first method often requires the expertise from the department of paediatrics since many departments of nuclear medicine are inexperienced with the Venflon procedure. That means that lot of time is needed before starting the renogram. The advantage is that the Venflon can be used for both tracer injection and furosemide injection at the end of the renogram and that extravasation is extremely rare. Moreover, the renogram can be started without a recent venous puncture that might provoke some fear in the child.

The second method is insertion of a needle into a peripheral vein. This has the advantage of being undertaken within the department of nuclear medicine by any skilful trained health personnel. Using a butterfly needle size 27/25 in a tiny vein (at the anterior side of the wrist or a scalp vein) results in many children not reacting to the injection. In many institutions anaesthetic cream (EMLA/Ametop) has been found unnecessary. After the injection is over, often the child will ask when will the injection be done.

Furosemide stimulation test

There are no data on the ideal time to administer the diuretic, a late (F +20) or an early injection (whether at F −15, or F 0 or even F +2) are acceptable.

Those in favour of the late injection prefer to observe directly the modification of the slope of the renogram following the furosemide injection. Furthermore, if partial emptying has occurred during the basic renogram (0–20 min), the administration of the diuretic can be avoided and only late PM views acquired.

The early furosemide injection has the advantage of reducing the acquisition time on the gamma camera. The F +2 is popular in those departments where more points are helpful for the calculation of the DRF when using the Patlak-Rutland plot. Although the curves might look completely different depending on the chosen option of furosemide injection, the final diuretic effect will be the same whatever the moment of furosemide injection as long as late PM data are acquired [45, 46].

Age for performing an initial renogram

The advantage of using a tubular tracer is that the quality of signal remains acceptable even in the very young infant. Generally, 1 month is considered as an acceptable time for performing the first renogram. In special cases, estimation of differential function can be carried out in the first week of life [7]. An example is in a case of huge postnatal hydronephrosis, where it is sufficient to know whether the kidney is working more or less normally, very abnormally or is not functioning at all. The result of the DRF will influence the surgical decision.

Timing for imaging/start of computer

Analysis of the renogram should start at the moment of the highest heart activity. Some parameters such as DRF or NORA need a clear, repeatable identification of the 1- to 2-min time interval. In those departments that have the possibility to adapt the processing to this requirement might comfortably start the computer some time before the injection of tracer. For those who do not, a good procedure is to inject the tracer first and, while looking to the screen, to start the computer when the tracer reaches the upper mediastinum.

Collimator

A low-energy all-purpose collimator is recommended. A dual-head camera is not recommended.

Position of detector

Position camera with the collimator facing up. The exception to this is in the patient who has undergone renal transplantation when an anterior scan is recommended.

Positioning of the child

Supine position will minimise renal depth difference and assist in keeping movement to a minimum. To reduce movement, support the child with either sandbags or Velcro straps on either side of the child or place the child in a vacuum cushion. When possible, the child should lie directly on the collimator surface. One must ensure that the heart, kidneys and bladder are all included in the field of view. Having the heart in the field of view is important if one is planning to use the Patlak-Rutland plot in the analysis of the renogram. Check the patient's position with a radionuclide marker to ensure that the lower chest (marker in axilla) and the entire abdomen (marker below pubic symphysis) are included in the field of view. In the tall adolescent, one might have to choose whether the heart or bladder should be included in the field of view.

Views

Posterior (except for transplanted kidneys).

Computer acquisition setup

Matrix: 128×128 and word (or byte) mode is recommended as the first choice, 64×64 matrix size and word mode being the second choice.

Zoom: A zoom for acquisition is recommended for paediatric studies, varying as function of body size.

Frame rate: All imaging sequences should preferably be performed using a 10-s frame time. Although the consensus on split function [4] considers that 10 as well as 20 s are acceptable, processing modes such as deconvolution, factor analysis (FA), OE and determination of the Patlak-Rutland plot (PR) require a 10-s frame time. The additional memory needed is not a problem anymore for all the gamma camera systems.

Whatever the processing method used, the DRF estimation is independent of frame time and will be the same using either 10- or 20-s frames [18, 19].

Duration of study: The basic renogram should have a minimal duration of 20 min.

If a furosemide stimulation test might be required, a separate 15- to 20-min acquisition is necessary. The advantage of this approach is that it allows checking first the renographic curves and then to decide whether or not a furosemide test is warranted. If there is a clear indication for a furosemide test already before the study begins, then some institutions prefer to inject the diuretic with or soon after the tracer. This acquisition should be for the minimum of 20 min.

The third sequence, in case of an insufficient renal emptying after the diuretic renogram, is a late post-erect PM dynamic acquisition that should be acquired using the same acquisition parameters as for the basic renogram and have a minimum duration of 2 min. Static PM images could be an alternative. The time of the PM should be standardised between 50 and 60 min, allowing a longer exposure to the diuretic, spontaneous voiding and a significant effect of gravity, the infant being held vertically in the parent's arms. It should NOT be performed immediately after the furosemide test, even if the child has had a spontaneous voiding during the two initial acquisitions.

Interventions

Diuretic administration (furosemide)

Dose: 1 mg/kg i.v. in infants, 0.5 mg/kg in children above the age of 1 year, with a maximum dose of 20 mg.
Timing of administration of furosemide: There are three variations.

- F +20: Furosemide is injected 20 min after the injection of tracer.
- F −15: Furosemide is injected 15 min prior to the tracer.
- F 0: Furosemide is injected at the beginning of the study. This method is gaining popularity since there is only a single i.v. injection, especially in the young child with small veins. In some departments using the Patlak-Rutland plot, the furosemide is given 2 min after the injection of tracer since the very quick transit of tracer through the kidney due to the effect of furosemide might invalidate the fitting process for estimation of DRF.

There is no evidence at the present time to suggest that any one of the above timings is "better" than the other. However, if there is difficult venous access then one single injection is to be recommended.

Post furosemide acquisition

Acquisition parameters: Use the same frame rate, zoom factor and matrix size as for the renogram.

Post micturition images

Positioning of the child: Supine, after the child has been upright for at least 15 min and has voided, the data should be acquired for 2 min.
Acquisition parameters: Dynamic acquisition using the same frame rate, zoom factor and matrix size as for the renogram.

Indications for the PM images

This series is essential at the end of the diuretic renogram if emptying is incomplete.

In children with known pathology in whom the need for a diuretic renogram is unlikely, PM images may be sufficient. In this case, the PM images may be acquired after the 0–20 min renogram. However, for consistency a PM image should be acquired 50–60 min after the injection of tracer; each institution should ensure that there is an attempt to standardise the entire renogram including the time frame. This will allow for comparison with sequential studies as well as comparison between different children (Table 1).

Table 1 Timing for acquisition

Time of diuretic administration	Duration of acquisition		
	Renogram	Post diuretic	PM images 50–60 min post tracer injection
F −15	20 min	–	2 min
F 0 or F +2	20 min	–	2 min
F +20	20 min	15–20 min	2 min

ACE inhibitors (captopril)

This is indicated in the presence of hypertension when renovascular disease is suspected. See guideline on ACE inhibitor renography [3]. See "Future perspectives" section.

Processing

These guidelines recognise that some departments may have a camera/computer processing system, which does not allow the current recommendations to be fulfilled. They must however be taken into account, and it is advisable to search for better software (see "Future perspectives" section). Prior to processing the data, quality control is essential. This includes checking for movement and possibly performing movement correction (see "Quality control" section).

Regions of interest

Every acquisition series should have ROI drawn.

Renal

The renal ROI must not cut the kidney or be drawn too close to the outer edge of the kidney. A too narrow renal ROI may let the scatter out of the ROI, neglecting therefore some significant renal activity. The operator needs to be generous [19–22].

The renal ROIs should be drawn on a summed image depending on the renal function (sum performed on a later series of images as renal function is decreased, in order to obtain a better signal to noise ratio) [41].

One may use isocontours, choosing the largest isocount line that follows the renal contour, each kidney being done separately. A manual ROI can also be used; an irregular shaped ROI offers no advantage over a rectangular box [19]. In case of huge accumulation of tracer in an extrarenal pelvis, the only method is to define an irregular ROI manually including both the early cortical activity and the extrarenal pelvis.

We would like to underline that the calculation of split renal function on a "cortical" ROI excluding the collecting system must be avoided. The renal images are a two-dimensional presentation of a three-dimensional object and therefore, behind and in front of the renal cavities, there is also renal parenchyma which needs to be included within the renal ROI.

Background ROI

The different background ROIs, which perform well according to published works, are:

- Rectangular
- Elliptical
- Surrounding the kidney outline, appropriately apart from the kidney (e.g. one or two pixels depending on the matrix size) to avoid scatter from the kidney activity. A perirenal ROI is the best compromise for the various components responsible for background activity in the renal areas [4]. In the presence of gross pelvic dilatation in the young infant, a perirenal background may not be possible since the kidneys extend virtually to the edge of the child; in such circumstances a background ROI above and below the kidney might be the best compromise.

  The two options that are unacceptable are either no background correction or a correction limited to the inferior/inferolateral renal area alone. In the case of asymmetrical DRF, this latter background ROI will result in significant overestimation of the worse functioning kidney [34].

Cardiac ROI

This ROI is needed for both the Patlak-Rutland fitting and for the calculation of OE. It should cover the hottest pixels over the heart on the very first two or three frames.

Background correction

Background correction should be applied to the renogram curves. If furosemide and/or the PM images have been acquired then these also require background correction. The background ROI counts must be size normalised to the kidney ROI, before subtraction from the kidney ROI counts [21–31].

Curve creation for each ROI

For every dynamic series there should be curve generation.

Renal curves corrected for background should be examined carefully. Ideally the corrected curve should pass

more or less through the origin of the x/y axes. Is there any fluctuation on the downslope, which might either suggest a reflux episode or movement? If it is due to movement then kidney, background and the heart curve will all show simultaneous fluctuation while reflux will usually affect only one renal curve. This fluctuation should be checked carefully with the entire sequence of images and differentiated from any pitfall such as, for instance, the progressive appearance of the bladder within the renal ROI.

Having the possibility of obtaining on a single image the curve profile of the three acquisitions, basic renogram, furosemide test and PM data will help both the nuclear medicine physician and the referring clinician in the interpretation of the renal drainage The estimated DRF should be compared with the early 1-2 min image (see below).

Images

A summed image of all the frames during the clearance or uptake phase, i.e. 60–120 s after the peak of the cardiac curve (vascular phase), should be created. This image reflects the regional parenchymal function and may allow the detection of regional abnormalities. Although ^{99m}Tc-dimercaptosuccinate (DMSA) is more appropriate for that purpose, one should not neglect the possibility of detecting parenchymal abnormalities when performing a renographic study [35]. Differential function should be visually assessed on this image and compared to the DRF estimated from the curves to ensure that there is congruity of results.

In addition, a series of timed images over duration of study should be created. The optimum is to add frames into 1-min images covering the duration of the study, including the PM images. All images should be displayed with the same scaling factor. The final display may include either 20 1-min images or the 1-, 2-, 10- and 20-min images plus an image of the late series.

With furosemide and the F +20 protocol, summed images over the duration of this post diuretic acquisition should be created with the same parameters as the images of the renogram and the same scaling factor. Functional images during the early phase may be useful.

Quantification

The minimum quantification data of a renogram should be the DRF (uptake phase) and excretion (third phase with response to furosemide if used).

Differential renal function

The relative function of each kidney is expressed as a percentage of the sum of the right and left kidneys. It is computed from the same time interval of the background-corrected renogram curves, this is 60–120 s from the peak of the cardiac (vascular) curve. No renal depth correction is required in children [33–35, 38]. This guideline recommends either the integral method or the Patlak-Rutland plot method [4, 20, 39–44]. If a diuretic has been given at the same time as the tracer or in the very young infant with an immature kidney, the rapid transit of the tracer through the kidney suggests that the DRF could be measured between 40 and 100 s.

The integral method: The parameter determined is the area under the background-corrected renogram, representing the total uptake during the selected time interval.

Although the differential function is usually calculated between 1 and 2 min, a quality control measure is to calculate the differential function for each frame separately during this time interval. If the differential function is constant (± 5%) from frame to frame this indicates the stability of this technique.

The Patlak-Rutland plot method (PR): The parameter estimated is the mean slope of the ascending portion of the curve plotting the background-corrected kidney ROI counts [R(t)] divided by the cardiac ROI counts [H(t)] as a function of the integral of the cardiac ROI counts divided by [H(t)]. In theory, this method is more accurate than the integral method, because of the added correction of the intrarenal vascular component. However, the PR method is based on a slope and as such is more sensitive to slight errors. The quality control of this method lies in the crucial necessity to visualise the actual slopes of the PR plot and the straight line fit to the slopes. This will ensure the optimum time interval (i.e. the best fit of the PR slopes) as well as the robustness of the DRF as the time points are moved. In the infant with immature function or in patients with a renal function impairment, the fluctuations of the PR plot might be so severe that no reliable time period can be chosen.

Obtaining the same DRF result (< 5%) with both the integral and the PR method will constitute a good quality control. Discordant results (difference≥5%) imply a need to check once again the entire processing, in particular the correctness of the renal and perirenal ROIs, as well as the quality of both the integral mean value and the PR fit.

When overall function is good and DRF falls between 40 and 60% then all methods work and will provide similar results. However, when global function is reduced and/or there is asymmetrical renal function then only these above methods have been recommended by the International Scientific Committee of Radionuclides in Nephrourology. There comes a

point however, when renal function is so impaired that no method can be recommended for assessment of DRF [43].

Excretion during renogram

Numerous methods to assess this phase have been referred to in the background section of this guideline. The simplest method is inspection of the curve. Normal excretion (early peak with a rapidly descending curve) as well as slightly delayed excretion are readily distinguished from abnormal excretion (continuously rising curve).

Diuretic response

Assessment of the response to the diuretic must include the analysis of the PM images and may be expressed in analysis of images, curve and numerical quantification.

Visual assessment of drainage can be achieved by reviewing the sequential 1-min images over the duration of the entire study, including the PM images using the same scaling. This is a subjective approach and is not quantifiable, but will give the first evaluation of the response to the diuretic challenge, e.g. no or almost no emptying, good emptying or partial emptying [45].

Quantification of the residual activity after the PM images [46, 47] can be achieved in one of the following ways. This guideline recommends using either NORA [50, 51] or OE [48, 49]; see "Interpretation of impaired drainage" section for details.

A recent study on interobserver reproducibility on drainage has shown that observers, looking to the same images and curves, may come to completely diverging results as far as the quality of drainage is concerned. Quantitative parameters, estimated on the late PM images, might help to improve the standardisation in interpreting the quality of drainage data [52, 53].

Quality controls: Adequate background correction is mandatory for both parameters [54]. For the calculation of NORA, one should define exactly the 1–2 min counts, the first frame corresponding to the peak of the heart curve. For OE, the integral of the heart curve has to be adapted to the initial part of the renogram. A visual representation of this procedure may help to increase the robustness of the number obtained.

- $T_{1/2}$ of the furosemide curve

  This parameter is not acceptable as an adequate tool for evaluating washout. The only situation in which it makes sense is in case there is a rapid and consistent decrease of the descending slope down to approximately zero. But in that unique situation, it is enough to decide on the shape of curve that the response to the diuretic was optimal.

  $T_{1/2}$ of the furosemide curve is an empiric parameter, depending not only on the last points of the curve but also on the initial points: if, for instance, significant drainage of tracer occurs during the basic renogram, then the post furosemide curve may be horizontal, resulting in a paradoxically prolonged $T_{1/2}$. Moreover, the data provided by the post-erect PM acquisition will very often contradict entirely the information provided by the $T_{1/2}$, the conclusion of "poor washout" being changed into "excellent washout".

  There are however no cutoff values available to differentiate between partial and poor emptying.

Results

The sequential images must be carefully reviewed and taken in conjunction with the curves and quantification data.

Hard copy output

The following is the minimum data set, which should be produced.

Time of injection

Must be stated in order to know the time of acquisition of the late series images relative to the injection of tracer.

Images

Series of timed images over duration of study and labelled right or left side should be produced. See "Images" section for details.

Regions of interest

These used should be displayed on a summed image.

Curves

Background-subtracted kidney curves over entire duration of study. Each kidney should be identified by colour or line structure.

Quantification

This should include the DRF calculated as per recommendations and T_{max} (time to peak). If drainage is unsatisfactory on the curves, one should try to provide some valuable quantification of the drainage (OE and/or NORA) at the end of the diuretic challenge (either F +20 or F 0) and especially on the late PM images.

Interpretation/reporting/pitfalls

Relative function: Normal values of DRF are between 45 and 55% uptake [4, 55]. DRF should be interpreted in clinical context, since values within the normal range may be seen also when there is bilateral renal damage and/or in the presence of chronic renal failure. Values outside this normal range may be seen when there is an uncomplicated unilateral duplex kidney as well as in unilateral renal damage.

Ectopic kidney: In the presence of an ectopic kidney, the DRF estimation will underestimate the function of the ectopic kidney in all cases. Either a ^{99m}Tc-DMSA scan with both posterior and anterior projection or a MAG3 renogram using a dual-head gamma camera and acquiring data on both heads is suggested in such cases. Drainage may be difficult to assess if the kidney lies close to or behind the bladder.

Images: The images should be reviewed. With the tubular agents the 60–120 s image may show a focal renal defect [35]. Dilated calyces and/or renal pelvis and/or a dilated ureter may be evident. Comparison between the renogram and PM images is important to assess the effect of a change of posture and micturition.

Drainage function: Good drainage is easy to define, since the images, curves and numerical data all reveal little tracer in the kidney and collecting system at the end of the study. Continuous increase of renal activity, even after furosemide and PM acquisition should lead to the conclusion of poor drainage. Unfortunately, poor drainage does not necessarily mean low urinary flow through a narrow segment. A very dilated renal pelvis, in particular in the immature or the poorly functioning kidney, can give rise in itself to such a poor drainage [56, 57]. For this reason the significance of reduced drainage is not an indication for surgery. These guidelines can only describe good and poor drainage and await further evidence on how best to define and interpret impaired drainage.

Quality control [52, 53]

1. Extravasation at the site of the injection may give rise to difficulties in processing the data. Extravasation may lead to incorrect interpretation of the study. The normal shape of the curves will be lost or reduced when extravasation has occurred.
2. Position of the child: Is the child straight, have the heart, kidneys and bladder been included in the field of view? A simple means for quality control is to run the study in cine mode. Patient movement, renal uptake of the tracer, transit from parenchyma to pelvis as well as drainage of the collecting systems are easily noted.
3. Adequate child immobilisation plus a helpful parent is better than any post acquisition data manipulation for motion. Check for patient motion using cine mode.

   If motion exists then an experienced operator is required to judge whether the movement is so marked that no numerical or graphical analysis is possible although viewing of the images may permit useful information from the study to be gained. With less movement, the operator may either use a large ROI on a summed image (over 1 min) or use a realignment program (using the manufacturer's software) [58, 59].
4. The beginning of the analysis of the study should be from the first frame when tracer is seen in the heart. Check that the computer was started early enough, i.e. no tracer is in the kidney on the first frame, but also that the computer was not started too early, i.e. no tracer on the first two to three frames. All timings should refer to the image where the cardiac (vascular) activity is highest.

Future perspectives

There is a need to have a standardised processing protocol that is easy to implement on any computer that allows data from all gamma camera manufacturers to be imported. Such a software package will allow an improved interobserver reproducibility, allow creation and evaluation of parametric images and allow a straightforward comparison of results from various centres. The International Atomic Energy Agency (IAEA) is in the process of generating such a package [60].

1. The definition of obstruction, or better, the definition of the risk factors of renal deterioration and therefore the operative indications are still a matter of debate. Ideally what the clinician requires is for the renogram to predict those kidneys really in danger or those who might improve their function after surgery. This would represent a main advance in paediatric renography. Only empirical attitudes are currently available, based on all kinds of combinations of clearance values, quality of drainage and degree of renal dilatation, which is fully discussed in an editorial [61]. At the present time, the renogram has been essentially an instrument to measure uptake function and drainage at entry and during conservative or postoperative follow-up.
2. Data manipulation of the renogram offers new possibilities:

   (a) The computer is able to generate pixel-by-pixel parametric images, based on the uptake function

using the Patlak-Rutland approach, as this has the advantage of a vascular correction. This image has been analysed in the context of renal scars, but has not been extensively studied in hydronephrosis. This might offer useful information about regional cortical impairment. This image needs to be evaluated in the context of clinical outcome and also be compared to the 1- to 2-min summed image.

(b) Recent work suggests that an impaired cortical transit, defined on a pure visual basis, might circumscribe those hydronephrotic kidneys, which left untreated, will deteriorate. Similarly, it might identify those kidneys with low DRF which could potentially improve after pyeloplasty [62]. This has still to be confirmed.

(c) At this moment, functional images based on cortical transit (T_{max} image, mean transit time image, factor analysis) have not shown to be useful to differentiate between simple dilatation and high probability of obstruction.

3. Techniques, which assess drainage relative to that kidney's uptake function:

   There are good software to assess drainage quantitatively, and data of both normal [48–50] and impaired or delayed [54, 63] renal excretion in paediatrics now exist. However, there are no data in children to allow interpretation of impaired drainage as obstruction [56, 57, 64, 65].

4. The volume of the renal pelvis is another variable, which cannot be taken into consideration using only diuretic renography; integration of post diuretic ultrasound volume measurements is one possible technique to determine this variable. How these results would then be incorporated with the results of the diuretic renogram remains to be worked out.

5. ACE inhibitor-enhanced studies:

   (a) Its use in case of arterial hypertension also requires further clarification.

   (b) In the presence of hydronephrosis, the possibility exists that DTPA renography with ACE inhibitors might distinguish those kidneys at risk compared to those kidneys that are stable and do not require intervention. This requires further research.

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