GUIDELINES FOR DIRECT RADIONUCLIDE CYSTOGRAPHY IN CHILDREN

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I 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 indications, acquisition, processing and interpretation of direct radioisotope cystography (DRC) in children.

The present document is inspired by the desire of the EANM and the American Society of Nuclear Medicine to have guidelines for most nuclear medicine procedures (1).

This guideline summarises the views of the Paediatric Committee of the European Association of Nuclear Medicine. The guideline should be taken in the context of "good practice" and any local/national rules, which apply to nuclear medicine examinations.

II Background and Definition

Vesicoureteral reflux (VUR) is a common abnormality found in children with urinary tract infection (UTI). In children with UTI different authors suggest an incidence of VUR between 22% to 52% (1,2,3,4,5).

With growth and maturation of the vesicoureteral junction up to 79% of VURs disappear spontaneously (6,7). VUR is more common in siblings of patients with VUR (8,9) and in children of parents with documented VUR (10). VUR is also found in renal transplant recipients and is one of the important etiologic factors of pyelonephritis in patients with transplanted kidney (11).

Cystography is undertaken to detect and follow up VUR (1,12,13,14,15). The generally accepted reference method is the radiological micturating cystogram (MCU) although the direct catheter radionuclide cystography (DRC) is probably more sensitive (16,17) and has a lower radiation burden than the MCU (5,18,19).

Direct ultrasound contrast enhanced cystography (DUSC) does not involve any radiation but requires a bladder catheter. Its image resolution is superior to radionuclide studies, but unlike DRC it does not permit a dynamic monitoring of filling and voiding phases concomitantly in both ureters and kidneys.

The indirect radionuclide cystogram (IRC) offers the possibility of detecting VUR without a bladder catheterization and allows micturition to be studied under physiological conditions. Some authors have shown high sensitivity of the IRC compared to DRC (26,27,28), but others have not been able to reproduce these results (29,30). Some institutions suggest those children > 3 years of age, who are toilet trained, should undergo an indirect cystogram prior to a DRC (28).

With MCU and DRC both the filling and micturition phases can be studied whereas only the micturition phase may be studied with the IRC and DUSC (20,25,26,27,28). Some studies demonstrated reflux only in the filling phase of the DRC

and suggested that imaging of the micturition phase only will miss reflux in a significant number of children [29,30].

DRC may be undertaken in any child, including infants; however a large bladder full of radionuclide may obscure the ureters, an ectopic kidney and rarely the renal pelvis in small babies.

Detection of VUR: VUR is an intermittent phenomenon, therefore reflux may not be detected at the time of DRC. Successive DRC, although performed with the same procedure, will not detect reflux constantly [31, 32, 33].

Evaluating any technique for the detection of VUR will remain difficult since there is no absolute reference method. Considering this fact cystography is contributory only when positive, whereas a negative examination cannot totally exclude VUR.

III Common Indications

Indications

Direct radionuclide cystography is indicated whenever detection of VUR is important. Main clinical indications are:

A. Detection of VUR in children after UTI (in boys the first catheter cystogram should be an MCU to visualise the urethra).
B. Follow up of children with known VUR during prophylactic antibiotic/bacteriostatic treatment
C. Assessment of the results of endoscopic or surgical treatment.
D. Screening of siblings of children/parents with proven VUR

DRC can be also used for the detection of VUR in renal transplant recipients and for serial evaluation of bladder dysfunction (e.g. neurogenic bladder) for reflux.

Contra indications

There are no contraindications. However children should not be catheterised during the active phase of UTI.

In the presence of low lying or pelvic kidney VUR may be missed if a dilated lower ureter is being investigated, then reflux into the lower ureter may not be detected, especially if the ureter empties with bladder emptying.

IV Procedure

A. Information about previous examinations relevant to this procedure

The clinical history, relevant biochemistry and urine analysis results, ultrasound data if available and previous radionuclide imaging should be reviewed.

B. Patient preparation

B.1 Information with appointment letter:

Full explanation of the DRC, which includes information on bladder catheterization, should be given to the parents/children in written form.

B.2 Prior to catheterization:

The procedure should be explained in detail to the child and parents again before beginning the study to obtain maximal co-operation from the child and parents during the study.

C. Precautions

The presence of a low or ectopic kidney makes the detection of reflux difficult or impossible because of the relationship of the ectopic kidney to the bladder. In such case there is no point in doing a study that cannot detect the abnormality for which one is looking.

A strict aseptic technique must be used for the catheterization. The risk of catheter induced infection is very small, approximately 0,2% [34]. Nevertheless, since kidneys in children are more vulnerable to infection, every child undergoing bladder catheterization should receive a prophylactic antibiotic. Usually a single dose of a peroral antibiotic, different from the one the child may already have, is sufficient. In case of

severe reflux a full intravenous treatment may be necessary. The catheter prophylaxis should follow local uro-nephrological praxis.

Foley's catheter should not be used.

D. Radiopharmaceutical

D.1 Radionuclide: Technetium-99m (^{99m}Tc).

D.2 Pharmaceutical: Labelled colloid or
DTPA (diethylene triamine pentaacetic acid) is preferred,
Pertechnetate ($TcO4^-$) can be used.

The bladder wall, especially in case of augmented bladder (inflammation), can absorb pertechnetate, which after entering the bloodstream can be excreted by the kidney and cause false positive result if accumulated in the collecting system [35]. The bladder wall does not absorb ^{99m}Tc-colloids or ^{99m}Tc-DTPA.

D.3 Dose schedule

20 – 40 MBq for 500 ml saline or
20 MBq for direct instillation technique.

D.4 Technique

Children are catheterized under aseptic conditions using a small size catheter (F6 or F8 feeding tube, according to child's size) and the bladder is emptied. Only adequately trained personnel should insert urinary catheters. It is advisable to put some anaesthetic gel into the urethra in boys a few minutes prior to catheterization.
In young children who are not toilet trained, a double disposable nappy is put in place to avoid contamination and the child is placed supine on the gamma camera face.

Two techniques may be used. Either mix the ^{99m}Tc tracer in 500 ml sterile isotonic saline warmed to body temperature and slowly fill the bladder under hydrostatic pressure. Filling of the bladder to capacity should take some 10 minutes. The container with the solution should be placed no higher than 40 – 60cm above the bladder level. Slow filling is mandatory to avoid an increase of bladder tone and premature micturition; pulsatile flow should also be avoided.

An alternative method is to start by instilling the full dose of radiotracer in a small volume into the bladder and then slowly fill the bladder with nonradioactive saline.

When bladder capacity is reached, or when the child shows urge to void or when there is cessation of flow from the bottle in a nonvoiding patient the filling is stopped and the child is allowed to void.

The volume used should not markedly exceed the formula for bladder volume:

Age x 30 + 30 cc = (Age in years + 1) x 30 cc.

Contamination should be prevented by using a urinary bag, bedpan and covering and padding of examination table with sufficient absorbing material. During the voiding phase in co-operative children the preferred position is sitting upright on the bedpan with the back to camera.
It is advisable to measure the voided volume with each micturition in toilet-trained children and the volume of radiotracer solution used if the first method (i.e. mixing ^{99m}Tc with saline) has been adopted.

Variants:
Cyclic DRC: Direct cystography is performed with several fillings of the bladder and micturitions. The catheter is not removed after the first voiding and the second filling is started through the same catheter. The data are recorded continuously from the beginning of the first filling until after the second or third voiding is completed. The sensitivity of the procedure is increased as compared with single filling technique [31].

DRC using suprapubic puncture: The bladder may be filled with radiotracer solution as described above

using suprapubic puncture instead of catheterization. Some consider this approach safer and less traumatic than direct bladder catheterization [36].

D.5 Radiation burden

Effective dose is approximately 0,048 mSv per 20 MBq of ^{99m}Tc.
The estimated dose to the bladder for the children between 1 and 10 years, and using 20 MBq of ^{99m}Tc per 500 ml, is 0,09 – 0,14 mGy, with an ovarian dose of 0,005 – 0,01 mGy and even smaller testicular dose [37, 38, 39].

Diluting the radiopharmaceutical in fluid before infusion and completely emptying the bladder after the examination [39] can reduce bladder dose. In rare cases when children cannot empty their bladder in front of camera, a bladder catheter could be used to empty the bladder, before they leave the department.

E. Image acquisition

E.1 Camera

Horizontal with the collimator facing up, followed by vertical, if the child is voiding in sitting position (see E.3 Patient position).

E.2 Collimator

General Purpose.

E.3 Patient position

Supine during both filling and voiding phase in the infant.
In the older, co-operative child the voiding is preferably done with the child sitting on the bedpan in front of the camera, which is now in a vertical position.

E.4 Views

Posterior.

E.5 Computer acquisition set up

Matrix: 64 x 64 or 128 x 128.

Zoom: Appropriate to include the area from symphysis pubis to the xyphoid in the field of view.

Dynamic/Static: Dynamic.

Frame rate: Maximum of 5 sec/frame.
If compressed images will be generated then 1sec/frame.

Duration of study: This will vary with the time it takes for the child to void. It is important that the dynamic acquisition begins simultaneously with beginning of filling of the bladder and is continued until micturition is complete.

F. Interventions

Not applicable.

G. Processing

Images are reviewed in cine mode as 5 seconds frames. This must be done carefully with the appropriate (low) window setting approximately 10 – 30 % of maximal bladder activity.

If the child remained reasonably still during the study ROIs over bladder and kidney regions can be drawn to generate time activity curves. A ROI over the ureteric region is usually not helpful, the images usually give clearer information about the status of the ureter.

The voided volume of urine can be measured (volume or weight), the count difference between the pre-void and post-void bladder curve may be converted to ml thus allowing the residual bladder activity as well as the volume of renal reflux in cc to be estimated [14, 16, 24]. Compressed image can be generated, if sequential images were acquired as 1 frame/sec (see V Issues requiring further clarification).

H. Hard copy output

Selected images showing reflux should be displayed in 5 sec/frame including micturition episode. In order for a reflux to be visualised the upper threshold may need to be lowered.

Time activity curves from bladder and kidney ROIs. The renal curves must either be displayed separately from the bladder or else the bladder curve must be rescaled so as not to overshadow the kidney curves.

If the voided volume has been measured this should appear as well as the calculated volume of reflux, if this has been observed.

A compressed image, representing bladder and each kidney separately may be displayed. (see V Issues requiring further clarification).

I. Interpretation/Reporting/Pitfalls

Reporting should be done directly on the computer screen. The diagnosis of VUR is based on an increase of activity in the renal pelvis, if changes in renal activity due to movement can be excluded; this should take all the different processing into consideration. When the images, curves and compressed image, if available, all show an increase of activity in the renal area the confidence of a positive diagnosis of reflux is high. Using only one parameter may lead to over reporting reflux especially when the images are viewed on a window with a very low threshold level. One should be careful not to interpret noise as kidney activity. No diagnosis of VUR should be made on the renal curves alone.

The classical appearance of VUR on the 5 seconds images will show the presence of activity in the renal pelvic area at any stage of the examination. The renal curve will also show an increase activity, commonly as bladder activity falls.

Radioactivity can be seen in the pelvic and/or ureteral regions also during filling of the bladder, when the child is straining to void, as well as during and after micturition. Frequently more than one appearance of activity in the renal collecting system is noted during one and the same study. It is important to note that the reflux is intermittent, only active, only passive or seen during filling and voiding, and if episodes of reflux correspond to bladder contractions (sign of a possible unstable bladder).

The presence of a low or ectopic kidney makes the detection of reflux difficult or impossible because of the relationship of the ectopic kidney to the bladder.

VUR on DRC cannot be graded according to the 5 classical radiological grades. For some clinicians, who use the grading of VUR to affect management this will be a drawback.

A simplified classification using only 3 grades is sometimes used [31, 40]. Since it is difficult and sometimes misleading to use the same terminology for the same condition using two different methods, i.e. contrast and radionuclide voiding cystography the following classification is proposed with approximate correlation with radiological grades.

Level of VUR	DRC grade	Radiological grade
Ureter	A	I
Pelvis	B	II and III
Pelvis, which appears dilated/ ureter appears dilated	C	IV and V

Evaluating any technique for the detection of VUR will remain difficult since there is no absolute reference

method. Considering the reservations on the sensitivity of any of the above mentioned methods, there is agreement that cystography is contributory only when positive, whereas a negative examination cannot exclude VUR.

J. Quality control

Movement of the child during acquisition. This may not allow meaningful curves to be generated but still allows visual assessment of the renal areas for VUR.

V Issues requiring further clarification

1. Movement correction

2. Quantification of post voiding residual bladder volume and refluxing volumes (RV), if present is possible if volume of urine voided or volume of fluid infused is measured. This requires regions of interest to be drawn over the bladder on pre- and postvoid images and number of counts in each ROI determined.

$$\text{RV (ml)} = \frac{\text{voided volume (ml) x postvoid bladder counts}}{\text{prevoid bladder counts} - \text{postvoid bladder counts}}$$

or

$$\text{RV (ml)} = \frac{\text{postvoid bladder counts x infused volume (ml)}}{\text{prevoid bladder counts}}$$

The bladder should be completely emptied before starting with infusion for accurate calculation of residual or refluxing volumes using the second method.

There is no consensus about the value of quantification of volumes. When calculated reflux volumes were compared to international contrast MCU grade for VUR there was no correlation between various VUR grades and volumes. Nevertheless some believe that this calculation is useful not only for the reflux volumes but also for the bladder capacity in order to detect bladder dysfunction.

3. A compressed image may be created if the data has been acquired in 1 sec/frame. This requires the entire area of the gamma camera to be divided into bladder region and the area above the bladder to be split into left and right, this will result in a compressed image of each kidney/ureter and bladder. The compressed image allows the entire study to be displayed as a single “histogram” with time on the X-axis, anatomy on the Y-axis and the degree of blackness of the grey scale representing the activity in the region.

The sensitivity of compressed images remains to be defined. Some departments consider this as a very sensitive index of VUR, however further work is required for clarification.

VI Concise Bibliography

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