Sources of error in direct radionuclide cystography in children and the need for a standardized, manometric apparatus

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Keywords: Radionuclide cystography - Manometry - Vesicoureteral reflux - Urinary tract infection

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Received:
18 November 2023
Accepted revised:
6 December 2023

Abstract
Direct radionuclide cystography (DRC) is a safe and reliable method for the detection and follow-up of vesico-ureteral reflux (VUR). Since the first DRC was performed, during the early 60s, the method has undergone many refinements. Themanometric approach, which was first introduced in 1984, provides a correlation between the bladder pressure and VUR visualization. In this study the sources of error that may alter the results of DRC are discussed and a novel, standardized low costmanometric apparatus is suggested.

Hell J Nucl Med 2023; 26(3): 219-223 *Epub ahead of print: 14 December 2023* *Published online: 28 December 2023*

Introduction

Direct radionuclide cystography (DRC) is a safe and reliable technique that is widely used for the detection and follow-up of vesico-ureteral reflux (VUR) [1]. Since 1963, when the first DRC was described by E.A. Dodge, the technique has been further improved [2]. In 1984, a manometric approach was introduced, providing a quantifiable criterion to the study i.e. the bladder pressure during the filling phase [3]. In fact, when the study includes assessment of the bladder pressure using a manometric apparatus (mDRC), some assumptions must be implemented.

Three common radiopharmaceuticals can be used in mDRC, technetium-99m (^{99m}Tc) sodium pertechnetate, ^{99m}Tc sulfur colloid, and sodium pertechnetate diethylene triamine penta-acetic acid (DTPA). For children 1-10 years old the estimated absorbed dose to the bladder, after the administration of 20MBq of pertechnetate is 0.09-0.14mGy [4]. The sensitivity of the method is 71%-100% and the specificity is 67%-100% [1,5].

Technique of mDRC

Prior to mDRC, bladder catheterization has to be performed by trained medical staff under aseptic conditions. In most cases, an F6 or F8 silicon feeding tube is used to empty the bladder. The application of 2% lidocaine gel into the urethra for the boys and in the genitalia for the girls before catheterization is recommended. The child is positioned supine on the gamma camera, immobilized and an absorbent paper is placed underneath the patient and on the camera's head to prevent radioactive contamination [6].

In nuclear medicine departments where mDRC is performed, a manometric apparatus using common-finding hospital equipment is used. A sample of such, connecting the patient's bladder catheter with a bottle of warm normal saline 0.9% (NS) is placed around 40-60cm above the level of the γ-camera bed, as described in Figure 1. Once in place, the radiotracer, diluted in 10mL of NS,is instilled through the catheter into the bladder and the study continues with the gradual filling of the bladder with NS up to the bladder's functional capacity which has been determined in advance. During the filling phase, sequential 5sec images are acquired, while bladder's pressure is measured periodically. The filling phase is terminated when the administered NS volume reaches or supervenes the predetermined functional capacity of the bladder; sometimes this may not be achieved due to various reasons and the filling phase gets completed when the child has the urge to void or when the flow from the NS bottle ceases as the differential pressure reaches zero.

After the filling phase has been completed, the child is asked to void either sitting or standing with his or her back facing the camera. Micturition chairs or similar devices can

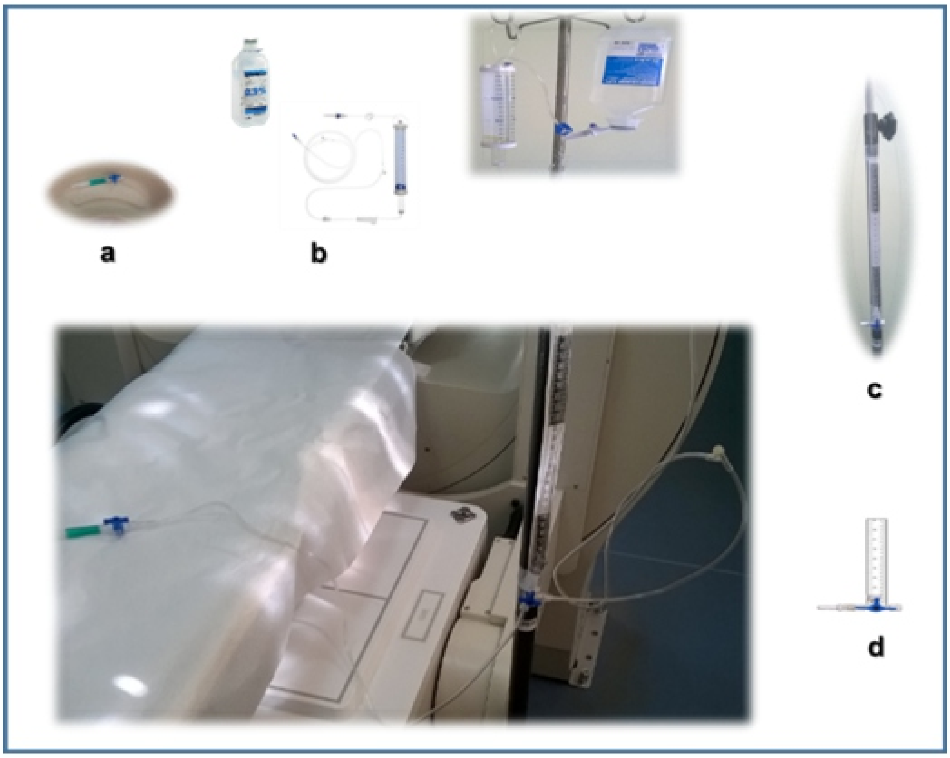

Figure 1. Manometric apparatus set up with easily-found hospital equipment. a) A 3-way stop cock connecting the 'zero-point' 3-way stop cock via the 'bladder' extension tubing and the bladder catheter via a straight infusion connector. b) The NS filling system consisting of a bottle of NS and an infusion burette connected to the 'zero-point' 3-way stop cock. c) The 'manometric' tubing, an extension tubing connected to the 'zero-point' 3-way stop cock, which is fixed in an upright position near a paper tape meter that is attached to a metallic stand) The 'zero-point' 3-way stop cock connecting the NS filling system, the 'manometric' tubing and the 'bladder' extension tubing. Note that the 'zero point' of the apparatus has been set to the level of the bladder (gamma-camera bed).

be used as well. It is usually recommended to measure the voided volume; in non-toilet trained children the voided volume can be measured by weighing the dipper prior and after micturition.

Sources of error

Common sources of error duringan mDRC study are:

1) Negative urine culture not submitted

The only absolute contra-indication for mDRC is urinary tract infection(UTI), therefore a recent (2-3 days prior) negative urine culture has to be submitted to the Nuclear Medicine department before the study. In case of existing lower UTI the possibility of retrograde flow of septic urine refluxing to the kidneys and causing pyelonephritis cannot be excluded.

In addition, if ^{99m}Tc sodium pertechnetate is used for the study in an inflammation setting, the tracer can be systemically absorbed through the inflamed bladder wall and visualized in kidneys, producing a false positive result as in a high grade VUR.

2) Parents/carers and patients not sufficiently informed

Parents and/or carers must be fully informed about all the steps of the study. Most anxious parents are adequately managed by nuclear medicine doctor's behavioral management skills, however in some cases a psychologist's help might be required. Depending on the child's age the procedure has to be explained either generally or more thoroughly. The discomfort of the study is usually well tolerated, when the child and the parents have been adequately informed and prepared. In anxious children, mild sedation can be used.

3) Collimator and equipment not covered

Manometric DRC involves handling a high radioactive urine volume under increased bladder pressure with the patient in a supine position, usually in children experiencing urgency to void. These conditions require proper preparation including collimator's covering prior to study, retain of a peaceful environment for the child and parents and precise manipulations by the personnel, in order to avoid radioactive contamination of gamma camera and other equipment.

4) Normal saline bottle not pre-warmed

The bottle of NS used for ladder filling must be warmed to body temperature. Administration of NS that has not previously been warmed could possibly result in a weak erdetrusor muscle contraction [7] or may elicit a contractile response, known as the bladder cooling reflex [8].

5) Normal saline bottle placed misplacement

The NS bottle is typically positioned approximately 40-60cm higher than the gamma camera's bed level, which corresponds to the bladder's level. In some departments the NS bottle is initially placed at an even higher level, sometimes up to 1 meter above the bladder's level, in order to ensure bladder's filling; however such a maneuver may lead to rapid filling of the bladder, which could result in delayed voiding [8]. In some cases, involving anxious older children or operated patients, bladder filling cannot either start or reach bladder functional volume required. In these cases, placing the

NS bottle up to 1 m than the gamma camera's bed level is considered acceptable, as long as the bladder filling process remains slow. The normal bladder filling rate should not exceed 50mL/min as it has been found that a filling rate of 50-100mL/min increases volume threshold for micturition and impairs the detrusor contractility [9].'

6) Zero point' placed at wrong level

The zero point of the manometric apparatus must be placed at the same level with the patient's bladder; if placed at a higher or a lower level, all pressure measurements will result to erroneous assessment.

7) Significantly lower/higher NS volume administered

The volume of NS administered must be close to the functional bladder capacity, as calculated using the formula: Bladder Volume (mL)=(age in years+1)x30. In our department the maximum volume difference allowed is set up to ±10%. If unilateral VUR has been already visualized in submaximal volumes, the study can be preferably continued near to the maximal bladder volume, if possible, in order to elucidate if VUR takes place to the contralateral ureter as well. If low-grade bilateral VURhas been visualized, especially during the first minutes of the study, DRC can be continued near to the maximal bladder volume, in order to clarify if VUR deteriorates. Only in cases where bilateral of highest grade VUR is visualized, the study can be terminated, regardless of the submaximal volumes administered. Deviations from these rules may lead to false positive results.

8) Radiotracer volume was ignored

The radiotracer is diluted in 10mL of NS and the practitioner instills the dilution into the patient's bladder through the catheter, before the beginning of the exam. In younger children, with small bladder capacity, the dilution volume is not negligible and must be taken into account when estimating the total filling volume, in order to avoid greater volume administration.

9) Rapid radiotracer instillation

Rapid instillation of the radiotracer could increase volume threshold for micturition. Instillation has to be performed slowly, during 1-2 minutes.

10) Voiding in wrong position

When a toilet-trained child is asked to sit or stand and void, the presence of the parents is needed in order to minimize embarrassment and avoid radio-contamination of the equipment. The most common mistake in such a demanding condition is to encourage a toilet-trained child to void while beingin a supine position. This results in suboptimal exams, since the gravity does not influence bladder emptying. A proper attitude of the department's personnel with fast and calm manipulations can ensure that the voiding phase will be properly performed with safety, in upright or sitting position.

Discussion

The main reason for performing a radioisotopic cystography is to successfully identify reflux of the urine into the ureter(s) and especially in renal pelvis(-es). However, in most cases this is the only finding eventually reported after thorough visual assessment of the sequential images of the study. Nowadays, after almost six decades of experience, there is still a variety of potentially useful information left unexploited during routine DRC studies performed without manometric devices. Moreover, assessment of the bladder pressure can be used to prevent bladder hyper distensionor insufficient filling of the bladder [3].

The few existing references about mDRC date back to the 80's [10, 11]. Moreover, there is no consensus to advice doctors and technologists. The European Association of Nuclear Medicine guidelines, printed approximately two decades ago, do not describe any relative manometric apparatus. Due to the lack of a certain, commercially available device or an officially approved manometric apparatus, for most nuclear medicine departments, mDRCremains challenging. In cases where such an apparatus exists, in some nuclear medicine departments, it is most likely that the technique is erroneously performed.

It is important to mention that the manometric apparatus used in mDRC represents a simple type piezometer, where the Gauge pressure at a point A inside the bladder is given by the equation: $PA= \rho \times g \times h$, where ρ is the mass density (Kg/m^3) of the liquid flowing through the tube, g is the acceleration due to gravity (m/s^2) and h is the rise of the liquid (m) in the piezometer glass tube. A sample of a simple piezometer is given in Figure 2.

A low cost apparatus, commercially available and easy to use, would make mDRC more appealing and precise tobe adopted. A sample of such an apparatus is depicted in Figure 3. Starting from the base, in order to be steady and safe, it must be metallic and fixed to a stand of adjustable height. The latter detail is absolutely a necessity, in order to set precisely the 'zero point' 3-way stop cock at the bladder level.

A ruler is placed vertically on the stand which measures up to 1 meter. At the base of the ruler, which we refer to as 'zero point', a 3-way stop cock is placed. Each outlet of this 3-way stop cock is connected to a glass tube. The vertical tube is used as an open-end manometer column, while the other two tubes are connected to the NS filling system and the bladder catheter.

The glass tubes used have to be inflexible, disposable, single-use and adjustable to 3-way stop cock. In particular, the vertical tube used has to be pre-calibrated from the manufacturer (40cm length proportional to 40cc volume) to ensure that one length unit on the ruler corresponds to one volume unit on the tube.

Glass is considered a smooth material with low friction; the friction between water and the walls of plastic tubes is generally higher than the friction between water and the walls of glass tubes. The use of glass tubes of same diameter prevents possible whirling of the NS circulating inside the manometric apparatus; the latter is important because turbulent flow of NS can affect the differential pressure measured.

In addition, tube inflexibility ensures that any external pressure which may influence readings on the manometer leading to false results, as it can happen when flexible plastic tubes used are bent, does not occur. Moreover, short, steady glass tubes can adequately retain the main piezometer assembly. When plastic tubes are used, since they are long

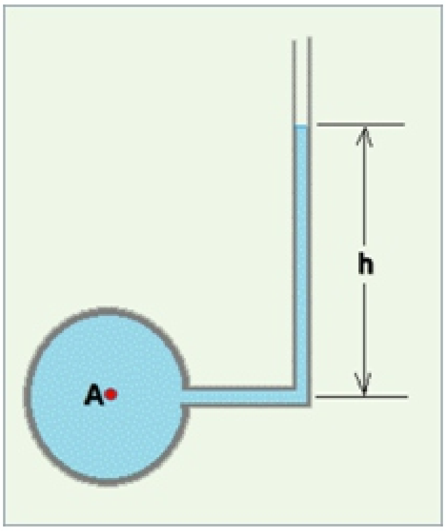

Figure 2. Simple piezometer tube. A is a point inside the bladder and h is the rise of the liquid in the piezometer glass tube.

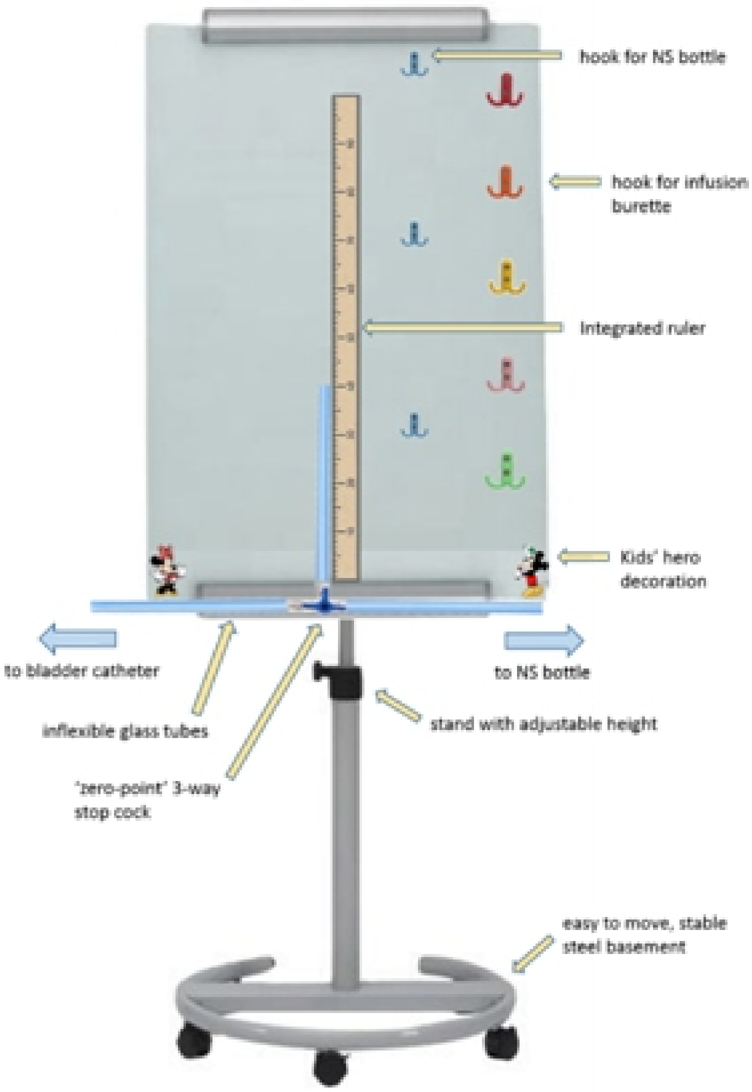

Figure 3. Sample of a convenient manometric apparatus.

and cannot be placed easily at the bladder level (see Figure 1), the manometer can be mistakenly converted either to a simple U-tube manometer or to an inclined U-tube manometer. The apparatus should also contain hooks for both the NS bottle and the infusion burette in various heights; finally, the apparatus can be decorated with children's heroes to distract little patients.

In conclusion, manometric DRC can provide valuable information about bladder pressure during the filling phase. However, when the examination is performed using easily-found hospital equipment it is usually time-consuming, challenging and subject to common errors, as described above. It is worth-mentioning that since mDRC is used to evaluate patients with VUR several times during childhood, standardization of mDRC study [12] performed in a nuclear medicine laboratory is probably more significant than obtaining precise measurements of bladder pressure. Knowledge of common sources of error can help to achieve state-of-the-art performance of this demanding nuclear medicine study. Along with this, the widespread use of a low cost, simple and easy to use manometric apparatus will contribute to minimizing the errors and increase the reliability of the results. By this way, mDRC can become patient-friendly and more appealing to doctors and technologists working in nuclear medicine departments. In that manner, future meta-analyses can use homogeneous data of standardized mDRC studies performed in a similar way globally and lead to helpful conclusions.

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