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Renal scintigraphic methods, which are physiologic and minimally invasive, have played important role in the management of various renal diseases in children, providing sensitive tool for early detection of disease even before structural changes become prominent and giving valuable functional and anatomical information to aid medical decision makings in the treatment and follow-up of patients. This review article focuses on the concept and advantages of renal scintigraphy in pediatric patients with various urologic diseases.

Key words: Renal scintigraphy, Pediatric nuclear medicine, Radioinuclide renography, Renal cortical scintigraphy, Diuretic renography

Introduction

Renal scintigraphic methods, which are physiologic and minimally invasive, have played important role in the management of various renal diseases in children, providing sensitive tool for early detection of disease even before structural changes become prominent and giving valuable functional and anatomical information to aid medical decision makings in the treatment and follow-up of patients. In this review article, general information regarding radiopharmaceuticals and techniques employed in performing renal scintigraphy is covered. Special consideration about radiation dosimetry in pediatric patients undergoing renal scintigraphic examination in nuclear medicine department is also included. Applications of renal scintigraphy in diagnosis and evaluation of various urologic problems are introduced.

Radiopharmaceuticals for renal scintigraphy

The radiotracers for the evaluation of renal drainage and excretory functions include ^{99m}Tc-MAG3 (mercaptoacetyltriglycine), ^{99m}Tc-DTPA (diethylene triamine pentacaetic acid), ^{123}I-OIH (ortho iodo hippurate), and ^{99m}Tc-GH (glucoheptonate). Technetium-99m–DMSA (dimercaptosuccinic acid) and ^{99m}Tc-glucoheptonate are tracers that accumulate in the renal parenchyme, which fit for static images. Most recently introduced radiotracer, ^{99m}Tc-(CO_3) NTA (tricarnonylnitriloacetic acid) is reported as having pharmacokinetic property similar to that of ^{123}I-OIH (ortho iodo hippurate)[9, 10].

1. ^{99m}Tc-MAG3 (Tubular secretion)

Technetium-99m-MAG3 is primarily excreted through active renal tubular transport, and its extraction fraction is 40-50%[1]. Because of its rapid renal clearance and primary excretion by the tubules on which furosemide acts, ^{99m}Tc-MAG3 is preferred over ^{99m}Tc-DTPA in patient with suspected obstruction or impaired renal function. And it is also recommended in pediatric patients unless calculation of GFR (glomerular filtration rate) is required, assuming that the absorbed radiation dose to those patients will be reduced in comparison to other renal tracers[2].

2. ^{99m}Tc-DTPA (Glomerular filtration)

Since ^{99m}Tc-DTPA is excreted primarily by glomerular filtration, it is the only imaging radiotracer available for the measurement of GFR[3]. Its extraction fraction is approximately 20%.

3. ^{123}I-OIH (Tubular secretion)

Iodine-123-OIH is cleared primarily by the proximal tubules. Its high uptake by renal tubules and rapid excretion into urine make this tracer useful for dynamic renal scintigraphy, though it is not routinely used due to its limited availability.

4. ^{99m}Tc-GH (Cortical retention and GFR)

About 40% of injected dose of ^{99m}Tc-GH is rapidly cleared into urine[4] by 1 hour and 8% to 10% of the initial tracer activity is present in the kidneys. It is suggested that this renal accumulation of ^{99m}Tc-GH, providing high-resolution cortical imaging, occur because it is actively concentrated in the proximal tubule by enzyme systems similar to those involved in PAH (para-aminohippurate) and hippuran transport[5].

5. ^{99m}Tc –DMSA (Cortical retention)

Technetium-99m-DMSA is the agent of choice for renal cortical scintigraphy. Using knockout mice lack of receptors essential to the proximal tubule endocytic uptake of proteins from the glomerular ultrafiltrate, the mechanism of renal uptake of ^{99m}Tc-DMSA is recently suggested as receptor-mediated endocytosis[6]. Uptake of ^{99m}Tc-DMSA is well correlated with renal blood flow and renal mass[7] and is widely used in pediatrics for the evaluation of relative renal function, pyelonephritis, and renal scarring[8].

6. ^{99m}Tc-(CO_3) NTA (Tubular secretion)

Technetium-99m-(CO_3)NTA is renal radiopharma-ceutical most recently developed[9]. The pharmacokinetic behavior of ^{99m}Tc-(CO_3) NTA was comparable to that of ^{131}I-OIH in the study included nine healthy volunteers[9] and in patients with chronic kidney disease[10]. More studies are needed to validate routine use of ^{99m}Tc-(CO_3) NTA as a renal tracer of choice for the measurement of effective renal plasma.

Radiation exposure

The radiation dose estimates calculated for the ^{99m}Tc-DTPA, ^{99m}Tc-MAG3, and ^{131}I-OIH in healthy adult volunteers were 0.0089, 0.010, and 0.089 mSv/MBq each on slow voiding protocol and were 0.0054, 0.0042, and 0.026 mSv/MBq on fast voiding protocol11 and these results suggest all estimates lie far lower than the average annual exposure from environment (reported as 2.4 mSv/MBq worldwidely, last updated on 13 Feb, 2013 via http://www.unscear.org). The effective radiation dose from plain chest radiography in neonate and pediatric patients varies from 0.016 to 0.02 mSv. Assuming ^{99m}Tc-MAG3 and ^{99m}Tc-DMSA are most commonly used radiotracers for renal scintigraphy in pediatric patients, nuclear medicine physicians and referring physicians need to be well informed of the radiation doses of these tracers in pediatric scale. In the study comparing radiation for pediatric nuclear medicine examinations following dose recommendation from NA (North Americal consensus guidelines)[13] and from EANM (European Association of Nuclear Medicine)[14], the effective dose of renal scintigraphy with ^{99m}Tc-MAG3 and ^{99m}Tc-DMSA calculated in pediatric patient varies from 0.40 mSv (in age of 1 year) to 1.83 mSv (in age of 15) depending on the guideline adopted (Table 1)[12]. Nuclear medicine physicians specially need to be aware of that the difference of radiation dose in two guidelines exists even in the same procedure, and be able to choose dosimetrically desirable one.

Techniques

1. Dynamic renal scintigraphy and renogram

Dynamic renal scintigraphy is acquired in two parts: rapid serial imaging immediately after bolus injection of radiotracer (^{99m}Tc-DTPA, ^{99m}Tc-MAG3, ^{99m}Tc-GH) to assess renal perfusion and acquisition of renogram to assess uptake of renal pharenchyme and clearance function. Additional pharmaceutical challenges may be applied in indicated patients, such as furosemide to acquire diuretic renography or captopril to acquire post-ACE (angiotensin converting enzyme) inhibitor study. The information regarding blood flow to the kidneys, renal cortical uptake, and clearance, represented in time activity curve (TAC), must be carefully interpreted in conjunction with visual inspection of images by expert nuclear medicine physicians as the curve and subsequently calculated parameters of renogram may be affected by many factors.

2. Static Renal Scintigraphy and renal cortical scintigraphy

With ^{99m}Tc-DMSA, planar renal scintigraphy is conventionally acquired as anterior, posterior, and left and right posterior oblique projection views. Magnification view using pinhole collimator is useful for examining the kidneys, providing more detailed view of cortical defects in pyelonephritis, infarction, and scarring. The relative renal function can be assessed according to the parenchymal uptake value of each kidney corrected for background activity (Fig. 1). In pediatric patients who require renogram curve and GFR estimation, this relative renal function can be calculated with ^{99m}Tc-DTPA instead[15], even though renal

Table 1. Radiation dose estimates for 3 common pediatric renal scintigraphic procedures with ^{99m}Tc-labeled tracers for adults and children at four different ages (Estimates from the study comparing radiation dose based on administered activities recommended by the EANM Dosage Card and 2010 NA consensus guidelines[12])

Age	1 year	5 years	10 years	15 years	Adult
Nominal weight (kg)	9.8	19	32	55	70
Dynamic renography					
^{99m}Tc-mercaptoacetyltriglycine (MAG3)	ICRP 80				
EANM administered activity (MBq)	23	33	45	61	70
EANM effective dose (mSv)	0.51	0.40	0.54	0.55	0.50
NA administered activity (3.7 MBq/kg)	37	70	118	204	259
NA effective dose (mSv)	0.81*	0.84*	1.42*	1.83*	1.81*
NA critical organ dose (mGy)-Bladder	1.2	1.3	2.0	2.8	2.8
Renal cortical scan					
^{99m}Tc-dimercaptosuccinic acid (DMSA)	ICRP 80				
EANM administered activity (MBq)	33	48	64	87	100
EANM effective dose (mSv)	1.22*	1.00*	0.96	0.96	0.88
NA administered activity (3.7 MBq/kg)	18	35	59	102	130
NA effective dose (mSv)	0.67	0.73	0.89	1.12	1.14*
NA critical organ dose (mGy)-Kidney	0.76	0.43	0.30	0.22	0.18
Radionuclide cystography					
^{99m}Tc-sodium pertechnetate	MIRD				
EANM administered activity (MBq)	20	20	20	20	-
EANM effective dose (mSv)	0.03	0.02	0.01	0.01	-
NA administered activity (3.7 MBq/kg)	37	37	37	37	-
NA effective dose (mSv)	0.06*	0.03*	0.02*	0.02*	-
NA critical organ dose (mGy)-Bladder	0.90	0.50	0.33	0.23	-

Calculation of effective dose and critical organ dose are based on ICRP80 (Radiation dose to patients from radiopharmaceuticals. A report of a Task Group of Committee 2 of the International Commission on Radiological Protection) and NUREG/CR-6345 (MIRD, Pediatric radiopharmaceutical administered doses: 2010 North American consensus guidelines).
Abbreviations: EANM, European Association of Nuclear Medicine; NA, North American; ICRP, International Commission on Radiological Protection; MIRD, Medical Internal Radiation Dose Committee
*Indicates the estimate is at least 20% greater than the dose calculated using the other (EANM or NA) consensus guideline as defined in the study by Grant FD et.al[12].

cortical scintigraphy with ^{99m}Tc-DMSA is regarded as most reliable method to evaluate relative renal function. SPECT (single photon emission computed tomography) permits simultaneous evaluation of images in all 3 (transverse, coronal, and sagittal) planes, which gives functional anatomical information definitely superior to planar scintigraphy.

GFR

Since accurate measurement of GFR is important for the evaluation of renal function especially in the pediatric oncologic patients when the chemotherapeutic regimen includes nephrotoxic drug[16] and also in the follow-up evaluation of patients with nephrourologic disease and of patients undergone surgery such as organ transplantation[17], several substances and methods were investigated in search of comparable substances and methods to that of inulin. Even though inulin is the best substance to measure GFR, many limitations of the procedure such as inconvenience, invasiveness, and in some cases, need of catheterization have hindered its active use in the mana-gement of patients. The most widely used radiopharma-ceutical for the purpose of measuring GFR, ^{99m}Tc-DTPA is primarily filtered by glomeruli with minimal tubular secretion and reabsorption and has a small amount of protein binding compared to that of inulin. Instead of tedious and invasive technique requiring blood sampling, the method based on renal uptake of ^{99m}Tc-DTPA detected with gamma camera may be more feasible for pediatric patients and will be discussed in this section. Using this camera based method, GFR is calculated after few minutes of imaging time without need of blood sampling and urine sampling. Even though there still exists concern about radiation, this simple, reliable, and non-invasive technique not only provides estimates of GFR itself, but also gives valuable parametric data such as relative kidney functions and critical information to differentiate between upper urinary tract dilation and structural obstruction, all of which can be simultaneously acquired from renogrpahy[18].

Clinical applications

1. Ureteopelvic junction obstruction

For an infant, 1month is generally accepted as reasonable time to undergo first renal scintigraphy. However, in case of severe hydronephrosis, if tracer like ^{99m}Tc-MAG3 which mainly extracted with tubular secretion is ideally used, the renal scintigraphy can be done even in the first week after birth, the results of which will aid urologists in timely decision making regarding surgical intervention[19]. As mentioned earlier, along with its favorable dosimetry, because of its higher clearance (40%) than that of ^{99m}Tc-DTPA, ^{99m}Tc-MAG3 provides superior diagnostic images and is an agent of choice for the renal scintigraphy in neonates and children. Since future deterioration of renal function cannot be predicted solely based on findings such as sonographically progressive dilation, obstruction, low differential function on diuretic scan[20], cortical transit

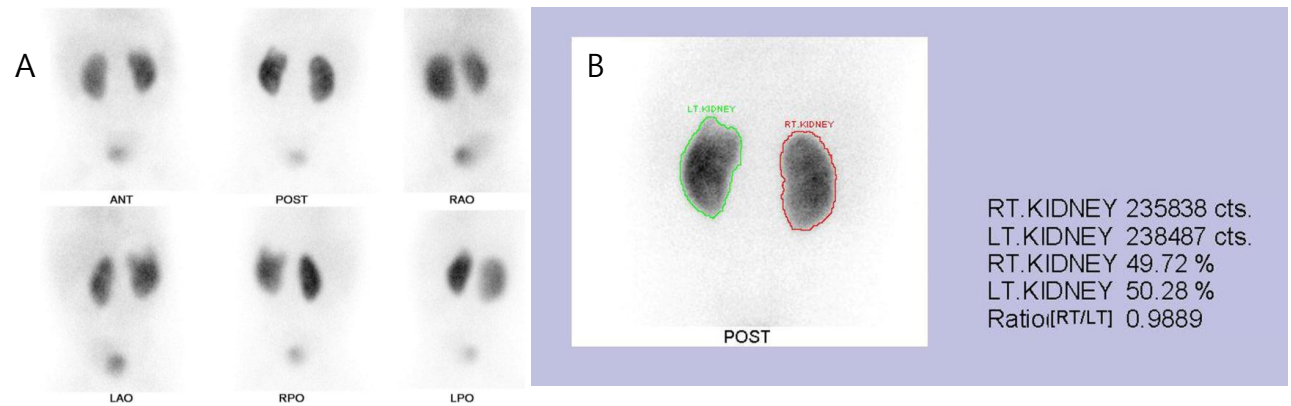

Fig. 1. The cortical defect demonstrated in ^{99m}Tc-DMSA planar renal scintigraphy. A) Focal cortical defect is noted in the upper pole of left kidney of 10 month-old male infant presented with acute febrile episode. B) The relative function is calculated from counts extracted in the region of interest (ROI) of each kidney.

time is expected to be a reliable predictive marker[21], and among many technical attempts to evaluate it, visual estimation of cortical transit seems to be the best approach[22]. Serial renal scintigraphy may help physicians in following-up of patients after therapeutic intervention. After unilateral pyeloplasty, patients with moderately impaired differential renal function serially estimated scintigraphically and patients diagnosed postnatally because of symptoms are suggested as those with the greatest likelihood of having a functional improvement[23].

2. Pyelonephritis

About 60% of children with febrile urinary tract infection (UTI) have scintigraphic finding of pyelone-phritis which is the most common serious bacterial infection in childhood[24]. Renal cortical scintigraphy with ^{99m}Tc-DMSA is more sensitive for the detection of pyelonephritis than sonography[25] and can be used in the acute phase of a UTI to confirm pyelonephritis, or from 6 to 12 months later to see if cortical scarring has been developed. With this technique, renal hypodysplasia can be detected and differentiated from scars related to UTI[24]. If the voiding cystoureterography (VCUG) is conducted based on scintigraphic evidence of pyeloneph-ritis during the acute phase of a UTI, cost and unnecessary distress associated with the procedure can be reduced.

3. Vericoureteral reflux

Vesicoureteral reflux (VUR), most important predisposing factor for UTI, may consequently lead to the complications such as renal scarring, hypertension, and chronic renal failure. Direct radionuclide voiding cystography (DRNC), the procedure causing 50-to 100-fold less radiation exposure to the gonads and bladder than VCUG[26], is helpful in diagnosis and follow-up of patients with VUR with higher sensitivity and higher temporal resolution than VCUG[27], even though accurate anatomical information of urethra and bladder and degree of reflux cannot be provided with DRNC. Besides its poor image resolution, DRNC has not been widely used probably because most urologists are familiar with the radiologic grading system[28]. In patients with hydronephrosis, abnormal findings on acute ^{99m}Tc-DMSA scan, and/or recurrent febrile UTI, VUR may be detected by DRNC in spite of normal VCUG result[26]. The prevalence of VUR in the siblings of children with VUR is reported as 27.4%, and the recommendation as a screening guideline in those population encompasses VCUG or radionuclide cystogram[29]. Considering lower radiation dose, performing DRNC preferentially is advisable since the information required in those children is the presence of VUR but not the detailed morphology of lower urinary tract.

4. Renal venous thrombosis

Although renal vein thrombosis is associated with low mortality, the outcome of renal function is not good[30], so these patients require close clinical follow up with serial sonography and ^{99m}Tc-DMSA scan[31]. Also, serial renal scintigraphy using ^{99m}Tc-MAG3 can be a sensitive method for the diagnosis and follow-up of these patients since renogram gives additional functional information regarding excretion. Typically, the findings of renal scintigraphy with ^{99m}Tc-MAG3 in renal venous thrombosis is presented as decreased perfusion, delayed cortical uptake, retention of radiotracer in the parenchyme, and no excretion.

5. Renovascular hypertension

Renovascular cause of hypertension comprise 5-10% of childhood hypertension[32]. In adults, sensitivity and specificity of renal scintigrpaphy combined with ACE inhibitor, captopril, for the diagnosis of renovascular hypertension is reported as high as 90%, respectively[33], even though there exist few published data in pediatric population (59-73% of sensitivity and 68-88% of specificity)[34, 35]. Precaptopril and post-captopril scintigraphy is recommended, depending on the availabi-lity and preferences, if primary investigation of secondary cause of hypertension has failed and blood pressure is not well controlled on 2 or more drugs [34]. Unilateral deterioration of the renogram curve or a change in relative function demonstrated by post-captopril study is highly suggestive of renovascular hypertension.

6. Renal transplantation

In assessment of function and complications, either parenchymal or structural, of renal graft, renal scintigraphy plays important role[36]. The pattern of perfusion, uptake, and excretion assessed with renal scintigraphy gives valuable information regarding early rejection, acute tubular

necrosis, and chronic transplant nephropathy[33]. The use of ^{99m}Tc-labelled mononuclear cells (WBC scan) may be considered for the diagnosis of acute rejection and for the differential diagnosis of ATN[37]. The use of renal scintigraphy in the diagnosis of acute complications associated with renal transplantation will be discussed in following section.

7. In acute care setting

1) Protocol in diuretic renography

The protocol adopting simultaneous injection of ^{99m}Tc-MAG3 and furosemide is advisable in the pediatric patients and especially in the acutely-ill patients, because it only takes about 20 to 25minutes to the completion of study as well as the protocol require only one injection. Better tolerance of patients and less radiation exposure can be expected with this approach[38].

2) Acute pyelonephritis

Even though renal cortical scintigraphy with ^{99m}Tc-DMSA plays critical role in detecting renal scar and phyelonephritis, the procedure takes hours, which might be inappropriate in acute care setting. Doppler ultrasonography has a low sensitivity of detecting acute pyelonephritis (APN)[39], and enhanced CT, despite of its high sensitivity, has risk of complications associated with contrast agents. Diuretic renal scintigraphy with short protocol adopting simultaneous injection of radiotracer and furosemide can be safely done with less radiation than enhanced CT, in short time, and without need of sedation in most cases. The typical finding of APN in diuretic renal scintigraphy, presented as regional parenchymal dysfunction, has reliable sensitivity as compared with renal cortical scintigraphy[40].

3) Urinary leak

Urinary leak can be caused by trauma or can occur as a complication after transplantation (anastomosis site, necrosis of distal ureter of transplant, etc) or as a consequence of iatrogenic injury. If additional information about other organ and/or bony structures is required as in the case of blunt trauma, CT is the modality of choice. However, in case of suspected urinary leak following transplantation or in patient allergic to the contrast media, multiple serial images of renal scintigraphy can effectively detect the presence of urinary leak and urinoma[41,42]. Renal scintigraphy with ^{99m}Tc-MAG3 can be used not only for the purpose of detection of urinary leak and urinoma, the study can also be used to differentiate urinoma from lymphocele or seroma.

4)Acute kidney injury

Assuming that there exist various causes (prerenal, intrinsic, postrenal) of acute kidney injury (AKI), identifying most probable insult as early as possible is nevertheless worth emphasizing. In patients with kidney transplant, early detection of AKI and rapid therapeutic management are essential to minimize the risk of graft loss. Renal scintigraphy can nicely demonstrate renal artery stenosis and infarct as perfusion defect and loss of uptake in affected area. Aforementioned scintigraphic findings of renal vein thrombosis can overlap with that of acute rejection. Diuretic renography has invaluable role in the detection of urinary tract obstruction in posttransplant patient. If prolonged renal cortical retention of radiotracer with relatively preserved perfusion is noted in renal scintigraphy, acute tubular necrosis (ATN) is suggested. Decreased perfusion, cortical uptake, and excretion of renal transplant is considered as typical scintigraphic pattern of acute rejection. The scintigraphic evaluation of renal transplant provides functional and anatomical information promptly with noninvasive procedure and with low radiation dose, so it can be readily chosen as imaging modality of renal transplant in pediatric patients especially in the acute care setting, before other invasive procedure such as needle biopsy is taken.

8. Other indications

Relative function of kidneys measured scintigraphically is useful for the evaluation of duplex, dysplastic, ectopic, and small kidney and for assessing remaining function preoperatively (Fig. 2).

Future prospective

Several attempts to develop new and powerful radiopharmaceuticals for functional renal imaging have been underway[43]. Among many potential PET (positron emission tomography) tracers targeting the angiotensin II subtype 1 receptor, ^{11}C-KR31173 is recently suggested as po-

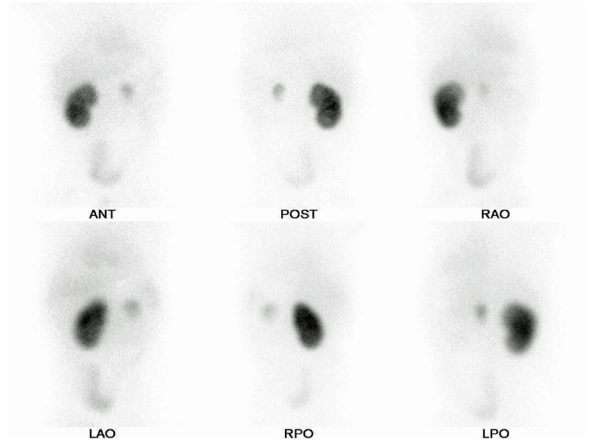

Fig. 2. Small sized left kidney with minimal uptake of ^{99m}Tc-DMSA. The uptake pattern and size of right kidney is within normal range (relative function of right kidney to left is measured as 95.99% to 4.01%).

tential imaging biomarker of renin angiotensin system activation and tissue injury in renovascular hypertension [44], use of which in human is expected in near future. In infants and children, since congenital obstructive nephropathy may cause renal failure in many cases, detecting obstruction in molecular level before serious structural and functional consequences take place will definitely contribute to the management of these patients. Candidates of target imaging molecules in assessing obstruction might be kidney injury molecule (KIM-1), Transforming growth factor beta 1 (TGF-β1), and monocyte chemoattractant protein-1 (MCP-1)[43]. A PET study with ^{18}F-PFH (ρ-[18F] fluorohippurate) in rats showed better quality compared with that of ^{99m}Tc-MAG3 and the parameters derived from this PET study seem to be close to that of ^{125}I- hippurate[45]. Evaluation of renal perfusion with O-15 labeled water can be done if on-site cyclotron is available for the production [46]. Rubidium-82 chloride (^{82}Rb) PET is recently suggested as a potential renal imaging agent[47]. The development of novel molecular imaging tracers with better performance for the diagnosis and management of urologic disease, which can be used safely and reliably in clinical routine, also in pediatric population, is eagerly anticipated.

Conclusions

Planar scintigraphy, SPECT, and PET are imaging modalities requiring administration of radiopharmaceutical. With intrinsic strengths of radiotracers such as excellent concentration to signal linearity, one-stop evaluation of whole body, and high specificity, these techniques make reliable functional assessment of kidney possible. The radiation exposure caused by renal scintigraphy is in most cases regarded as negligible, which is about one-third of the average annual exposure of naturally existing radiation sources in adult. And in many instances, renal scintigraphy is actively implemented as critical method for diagnosing and evaluating various urologic problems in pediatric patients without concerns about toxic or pharmacologic side effects and allergic reactions. Perception of utility and benefit of radionuclide renal scintigraphy by urologist as well as the nuclear medicine physician's effort to tailor protocols to the high standard and to interpret results meticulously are of importance in the effective application of the modality in urologic diseases.

Conflict of interest

No potential conflict of interest relevant to this was reported.

Referecnes

1. Bubeck B, Brandau W, Weber E, Kalble T, Parekh N, Georgi P. Pharmacokinetics of technetium-99m-MAG3 in humans. J Nucl Med 1990;31:1285-93.
2. Conway JJ, Maizels M. The "well tempered" diuretic renogram: a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis. A report from combined meetings of The Society for Fetal Urology and members of The Pediatric Nuclear Medicine Council--The Society of Nuclear Medicine. J Nucl Med 1992;33:2047-51.
3. Klopper JF, Hauser W, Atkins HL, Eckelman WC, Richards P. Evaluation of 99m Tc-DTPA for the measurement of glomerular filtration rate. J Nucl Med 1972;13:107-10.
4. Arnold RW, Subramanian G, McAfee JG, Blair RJ, Thomas FD. Comparison of 99mTc complexes for renal imaging. J Nucl Med 1975;16:357-67.
5. Lee HB, Blaufox MD. Mechanism of renal concentration of technetium-99m glucoheptonate. J Nucl Med 1985;26:1308-13.
6. Weyer K, Nielsen R, Petersen SV, Christensen EI, Rehling M, Birn H. Renal uptake of 99mTc-dimercaptosuccinic acid is dependent

on normal proximal tubule receptor-mediated endocytosis. J Nucl Med 2013;54:159-65.

7. Daly MJ, Jones W, Rudd TG, Tremann J. Differential renal function using technetium-99m dimercaptosuccinic acid (DMSA): in vitro correlation. J Nucl Med 1979;20:63-6.
8. Piepsz A, Colarinha P, Gordon I, Hahn K, Olivier P, Roca I, et al. Guidelines for 99mTc-DMSA scintigraphy in children. Eur J Nucl Med 2001;28:BP37-41.
9. Taylor AT, Lipowska M, Marzilli LG. (99m)Tc(CO)3(NTA): a (99m)Tc renal tracer with pharmacokinetic properties comparable to those of (131)I-OIH in healthy volunteers. J Nucl Med 2010;51: 391-6.
10. Taylor AT, Lipowska M, Cai H. 99mTc(CO)3(NTA) and 131I-OIH: comparable plasma clearances in patients with chronic kidney disease. J Nucl Med 2013;54:578-84.
11. Stabin M, Taylor A, Jr., Eshima D, Wooter W. Radiation dosimetry for technetium-99m-MAG3, technetium-99m-DTPA, and iodine-131-OIH based on human biodistribution studies. J Nucl Med 1992;33:33-40.
12. Grant FD, Gelfand MJ, Drubach LA, Treves ST, Fahey FH. Radiation doses for pediatric nuclear medicine studies: comparing the North American consensus guidelines and the pediatric dosage card of the European Association of Nuclear Medicine. Pediatr Radiol 2014.
13. Gelfand MJ, Parisi MT, Treves ST, Pediatric Nuclear Medicine Dose Reduction Workgroup. Pediatric radiopharmaceutical administered doses: 2010 North American consensus guidelines. J Nucl Med 2011;52:318-22.
14. Lassmann M, Biassoni L, Monsieurs M, Franzius C, Jacobs F, Eanm Dosimetry Paediatrics Committees. The new EANM paediatric dosage card. Eur J Nucl Med Mol 2007;34:796-8.
15. Celik T, Yalcin H, Gunay EC, Ozen A, Ozer C. Comparison of the Relative Renal Function Calculated with 99mTc-Diethylenetriaminepentaacetic Acid and 99mTc-Dimercaptosuccinic Acid in Children. World J Nucl Med 2014;13:149-53.
16. Gibson P, Shammas A, Cada M, Licht C, Gupta AA. The role of Tc-99m-DTPA nuclear medicine GFR studies in pediatric solid tumor patients. J Pediatre Hematol Oncol 2013;35:108-11.
17. Filler G, Sharma AP. How to monitor renal function in pediatric solid organ transplant recipients. Pediatr Transplant 2008;12:393-401.
18. Gutte H, Moller ML, Pfeifer AK, Thorup J, Borgwardt L, Kristoffersen U S, et al. Estimating GFR in children with 99mTc-DTPA renography: a comparison with single-sample 51Cr-EDTA clearance. Clin Physiol Funct Imaging 2010;30:169-74.
19. Piepsz A. Antenatal detection of pelviureteric junction stenosis: main controversies. Semin Nucl Med 2011;41:11-9.
20. Chiou YY, Chiu NT, Wang ST, Cheng HL, Tang MJ. Factors associated with the outcomes of children with unilateral ureteropelvic junction obstruction. J Urol 2004;171:397-402; discussion
21. Piepsz A, Tondeur M, Nogarede C, Collier F, Ismaili K, Hall M, et al. Can severely impaired cortical transit predict which children with pelvi-ureteric junction stenosis detected antenatally might benefit from pyeloplasty? Nucl Med Commun 2011;32:199-205.
22. Harper L, Bourquard D, Grosos C, Abbo O, Ferdynus C, Michel JL, et al. Cortical transit time as a predictive marker of the need for surgery in children with pelvi-ureteric junction stenosis: preliminary study. J Pediatr Urol 2013;9(6 Pt B):1054-8.
23. Castagnetti M, Novara G, Beniamin F, Vezzu B, Rigamonti W, Artibani W. Scintigraphic renal function after unilateral pyeloplasty in children: a systematic review. BJU Int 2008;102: 862-8.
24. Montini G, Tullus K, Hewitt I. Febrile urinary tract infections in children. N Engl J Med 2011;365:239-50.
25. Taylor AT. Radionuclides in nephrourology, part 1: Radiopharmaceuticals, quality control, and quantitative indices. J Nucl Med 2014;55:608-15.
26. Dalirani R, Mahyar A, Sharifian M, Mohkam M, Esfandiar N, Ghehsareh Ardestani A. The value of direct radionuclide cystography in the detection of vesicoureteral reflux in children with normal voiding cystourethrography. Pediatr Nephrol 2014;29:2341-5.
27. Polito C, Rambaldi PF, La Manna A, Mansi L, Di Toro R. Enhanced detection of vesicoureteric reflux with isotopic cystography. Pediatr Nephrol 2000;14:827-30.
28. Piepsz A, Ham HR. Pediatric applications of renal nuclear medicine. Semin Nucl Med 2006;3:16-35.
29. Skoog SJ, Peters CA, Arant BS, Jr., Copp HL, Elder JS, Hudson RG, et al. Pediatric vesicoureteral reflux guidelines panel summary report: Clinical practice guidelines for screening siblings of children with vesicoureteral reflux and neonates/infants with prenatal hydronephrosis. J Urol 2010;184:1145-51.
30. Mocan H, Beattie TJ, Murphy AV. Renal venous thrombosis in infancy: long-term follow-up. Pediatr Nephrol 1991;5:45-9.
31. Piscitelli A, Galiano R, Piccolo V, Concolino D, Strisciuglio P. Successful management of neonatal renal venous thrombosis. Pediatr Int 2014;56:e65-7.
32. Wyszynska T, Cichocka E, Wieteska-Klimczak A, Jobs K, Januszewicz P. A single pediatric center experience with 1025 children with hypertension. Acta Paediatr 1992;81:244-6.
33. Taylor AT. Radionuclides in nephrourology, Part 2: pitfalls and diagnostic applications. J Nucl Med 2014;55:786-98.
34. Tullus K, Brennan E, Hamilton G, Lord R, McLaren CA, Marks SD, et al. Renovascular hypertension in children. Lancet 2008;371: 1453-63.
35. Ng CS, de Bruyn R, Gordon I. The investigation of renovascular hypertension in children: the accuracy of radio-isotopes in detecting renovascular disease. Nucl Med Commun 1997;18:1017-28.
36. Gencoglu EA, Moray G, Karakayali H, Emiroglu R, Haberal M. The value of quantitative Tc-99m diethylenetriamine pentaacetic acid scintigraphy for assessing pediatric renal transplant recipients. Transplant Proc 2003;35:2630-3.
37. Lopes de Souza SA, Barbosa da Fonseca LM, Torres Goncalves R, Salomao Pntes D, Holzer TJ, Proenca Martins FP, et al. Diagnosis

of renal allograft rejection and acute tubular necrosis by 99mTc-mononuclear leukocyte imaging. Transplant Proc 2004;36:2997-3001.

38. Sfakianakis GN, Sfakianaki E, Georgiou M, Serafini A, Ezudding S, Kuker R, et al. A renal protocol for all ages and all indications: mercapto-acetyl-triglycine (MAG3) with simultaneous injection of furosemide (MAG3-F0): a 17-year experience. Semin Nucl Med 2009;39:156-73.
39. Yoo JM, Koh JS, Han CH, Lee SL, Ha US, Kang SH, et al. Diagnosing acute pyelonephritis with CT, Tc-DMSA SPECT, and doppler ultrasound: A comparative study. Korean J Urol 2010;51:260-5.
40. Sfakianakis GN, Cavagnaro F, Zilleruelo G, Abitbol C, Montane B, Georgious M, et al. Diuretic MAG3 scintigraphy (F0) in acute pyelonephritis: regional parenchymal dysfunction and comparison with DMSA. J Nucl Med 2000;41:1955-63.
41. S. T. Trevis MD. Pediatric Nuclear Medicine/PET: Springer New York; 2007.
42. Son H, Heiba S, Kostakoglu L, Machac J. Extraperitoneal urine leak after renal transplantation: the role of radionuclide imaging and the value of accompanying SPECT/CT - a case report. BMC Med Imaging 2010;10:23.
43. Szabo Z, Alachkar N, Xia J, Mathews WB, Rabb H. Molecular imaging of the kidneys. Semin Nucl Med 2011;41:20-8.
44. Xia J, Seckin E, Xiang Y, Vranesic M, Mathews WB, Hong K, et al. Positron-emission tomography imaging of the angiotensin II subtype 1 receptor in swine renal artery stenosis. Hypertension 2008;51:466-73.
45. Pathuri G, Sahoo K, Awasthi V, Gali H. Renogram comparison of p-[(18)F]fluorohippurate with o-[(125)I]iodohippurate and [(99 m)Tc]MAG3 in normal rats. Nucl Med Commun 2011;32:908-12.
46. Koivuviita N, Liukko K, Kudomi N, Oikonen V, Tertti R, Manner I, et al. The effect of revascularization of renal artery stenosis on renal perfusion in patients with atherosclerotic renovascular disease. Nephrol Dial Transplant 2012;27:3843-8.
47. Tahari AK, Bravo PE, Rahmim A, Bengel FM, Szabo Z. Initial human experience with Rubidium-82 renal PET/CT imaging. J Med Imaging Radiat Oncol 2014;58:25-31.