Annals of Nuclear Medicine Vol. 8, No. 2, 147–152, 1994

A comparative study of evaluating renal scars by ^{99m}Tc-DMSA planar and SPECT renal scans, intravenous urography, and ultrasonography

Tzu-Chen YEN,* Wei-Perng CHEN,** Shu-Lian CHANG,* Yan-Cherng HUANG,* Chung-Pin HSIEH,*** Shih-Hwa YEH* and Ching-Yuang LIN**

*Departments of *Nuclear Medicine and **Pediatrics, Veterans General Hospital-Taipei and National Yang-Ming Medical College*
****Department of Pediatrics, Taipei Municipal Women's and Children's Hospital*

The purpose of this prospective study is to compare 3 types of ^{99m}Tc-DMSA renal scan [(a) planar, (b) x-ray type film static SPECT presentation (SPECT-1) and (c) dynamic three-view display of SPECT slices (SPECT-2)], intravenous urography, and ultrasonography in the diagnosis of renal scars. All these studies were performed in 130 pediatric patients, with urinary tract infection (42 patients), vesicoureteral reflux (37), and unilateral or bilateral small kidney(s) (51). The number of renal scars detected was highest with the ^{99m}Tc-DMSA renal SPECT-1 scan and next came the ^{99m}Tc-DMSA renal SPECT-2 studies. There is a significant difference ($p < 0.05$) between the ability of planar and SPECT-1 to recognize renal defects. However, SPECT-2 may provide the best stereotactic localization and image quality of all the methods.

Key words: Tc-99m DMSA, SPECT, IVU (Intravenous urography), ultrasonography, renal scar

INTRODUCTION

THE DIAGNOSIS of renal scarring is very important for the pediatric patient because it has been associated with the later development of hypertension, kidney failure, and end-stage kidney disease.[1] Although the etiology of renal scarring is still not clear, some reports show that it bears on recurrent urinary tract infection and vesicoureteral reflux.[2–4] For many years intravenous urography (IVU) was considered the best method to use in diagnosing renal scar, however, recent studies indicate that the sensitivity and specificity of the ^{99m}Tc-dimercaptosuccinic acid (DMSA) renal scan are better than IVU, especially in detecting early stage renal scar.[5–8] Although ultrasonography is noninvasive, nonionizing, relatively inexpensive and very convenient, its role in the early diagnosis of renal scar is limited.[6,9]

Various studies have compared the sensitivity of the ^{99m}Tc-DMSA renal scan, IVU, and ultrasonography in detecting renal scarring.[6,10–16] Although these studies usually showed that ^{99m}Tc-DMSA was the most sensitive procedure, and emphasized their complementary nature, some included the following conditions or limitations which may have modified the results. These were avoided in the present work. Dillon et al.[10] studied selected subjects who had a small and contracted kidney and renal hypertension. The results of Verber et al.[11] were based on opinions from different pediatricians and hence were perhaps inconsistent. The ^{99m}Tc-DMSA renal scan used in these three studies was planar only. These limitations were avoided in the present work. Although the role of x-ray film type single photon emission computed tomography (SPECT-1) in the ^{99m}Tc-DMSA renal scan has been described,[17] few applications have been reported, although SPECT has been shown to detect children's renal cortical defects not diagnosed by planar scintigraphy.[18] It is believed that dynamic three-view display SPECT slices (SPECT-2) have not previously been used with ^{99m}Tc-DMSA renal scans, although they have proved to be a useful diagnostic method[19] in detecting liver hemangiomas.

The aim of our research is to extend the previous studies[6,10–16] and we assess and discuss the value of ^{99m}Tc-DMSA renal scans using SPECT-1 and SPECT-2.

MATERIALS AND METHODS

Patients: This study was done from Aug. 1, 1992 to July 30, 1993. One hundred and thirty patients were referred by the pediatric nephrologists of the Veterans General Hospital-Taipei and Taipei Municipal Women's and Chil-

Received November 29, 1993, revision accepted February 23, 1994.

For reprint contact: Dr. Tzu-Chen Yen, Department of Nuclear Medicine, Veterans General Hospital-Taipei, Taipei, Taiwan 11217, REPUBLIC OF CHINA.

Table 1 Clinical data of the patients included in this study

Clinical diagnosis	Patient Numbers (M/F)	Mean age (yr)*
Urinary tract infection	42 (23/19)	1.8 ± 0.8
Vesicoureteral reflux	37 (22/15)	4.9 ± 2.7
Unilateral or Bilateral small kidney(s)	51 (28/23)	7.4 ± 2.1

*mean ± 1 sd (in years)

dren's Hospital with the following diagnoses: 1) urinary tract infection (UTI) (42 patients), 2) vesicoureteral reflux (37), and 3) unilateral or bilateral small kidney(s) (51) (Table 1). The patients with UTI were imaged within 3 days of the diagnosis being confirmed by positive urine culture. All patients underwent ^{99m}Tc-DMSA renal scans (planar, SPECT-1, and SPECT-2), IVU, and ultrasonography and all these examinations were completed within one week. Sedation was required very rarely, for the radiographers were experienced in handling pediatric patients.

Intravenous urography: The IVU procedure was done without any prior bowel preparation or fluid restriction. All studies were performed with non-ionic contrast medium (Omnipaque300; Winthrop Laboratories, New York, N.Y.) at a dose of 2 ml/kg with a minimum dose of 10 ml and a maximum dose of 40 ml. Each study comprised 4 plain films with no additional tomography of the kidneys. A scar was defined as a focal area of narrowing, deformity, or both, of the renal parenchyma, usually associated with deformity of an adjacent calix.

Ultrasonography: The renal images were obtained from an ATL Ultra Mark 8 machine with a 5 MHz transducer. At least nine images were obtained of different portions of each kidney including three parasagittal views, three transverse views and three coronal views. A scar was defined as an area of cortical thinning with or without depression of the cortical margin.

DMSA scan method: The ^{99m}Tc-DMSA was prepared from a commercial kit (Daiichi, Japan) and the ^{99m}Tc-DMSA dose was based on the adult dose of 100 MBq and corrected for the patient's age in years by means of the following formula:

$$\text{Dose} = \frac{(\text{age} + 1) \times \text{adult dose}}{(\text{age} + 7)}$$

The minimum dose was 40 MBq.[19]

Imaging was performed 3 h after injection of ^{99m}Tc-DMSA. All studies were performed on an APEX SP-4HR (Elscint, Haifa, Israel) digital gamma camera with interfaced computer. Planar images were acquired first, in the anterior and posterior projections with a total of 300000 counts per image using a low-energy, all-purpose collimator. SPECT images were obtained immediately after planar imaging and used 60 projections with 20 s per stop. Following the application of a Matz pre-filter, transverse images were reconstructed with backprojection and a ramp filter. Coronal and sagittal views with respect to the patient were reconstructed from transverse slices without any additional filtering. The SPECT-1 method comprised evaluation of a side by side static display of image slices in transverse, sagittal and coronal directions. This is also known as the "conventional static method". The dynamic display method (SPECT-2) also displays images in the same three orthogonal planes, side by side, one cross section per view, but allows for ciné display and sequential step by step viewing through the slice set. The position of each slice of the group of three viewed simultaneously is identifiable by a marker on the other two. These studies were reviewed by three radiologists and nuclear physicians in random order without knowledge of the diagnosis or lesion location. The diagnosis and degree of scar severity were confirmed by at least two of the three interpreters. The degree of severity for all methods was on the scale 0–8 according to the criteria of Monsour et al.,[20] which included combinations of the presence of cortical flattening, definite localized defect (one or multiple) in one or both kidneys and shrunken kidneys.

Table 2 A comparative study for evaluation of a total of 473 renal scars by ^{99m}Tc-DMSA planar, SPECT-1 and SPECT-2 renal scans, IVU, and ultrasonography

	^{99m}Tc-DMSA			IVU	Ultrasonography
	Planar	SPECT-1	SPECT-2		
sensitivity (%)	90	96	92	85	75
scar number	426	454	435	402	355

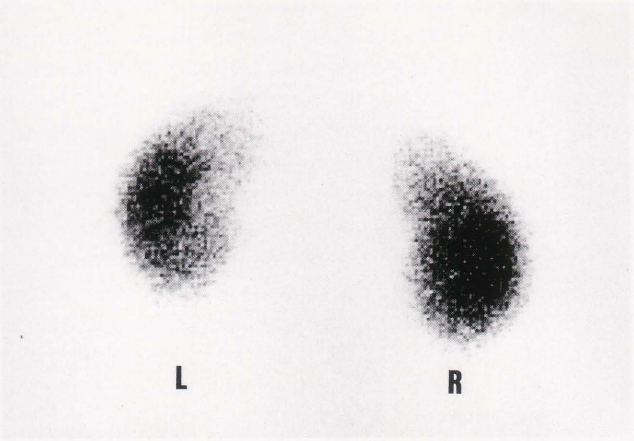
Statistical analysis: All statistical analyses were performed by ANOVA-square analysis for categorical variables and the t test for the continuous variable. $P < 0.05$ level was regarded as statistically significant.

RESULTS

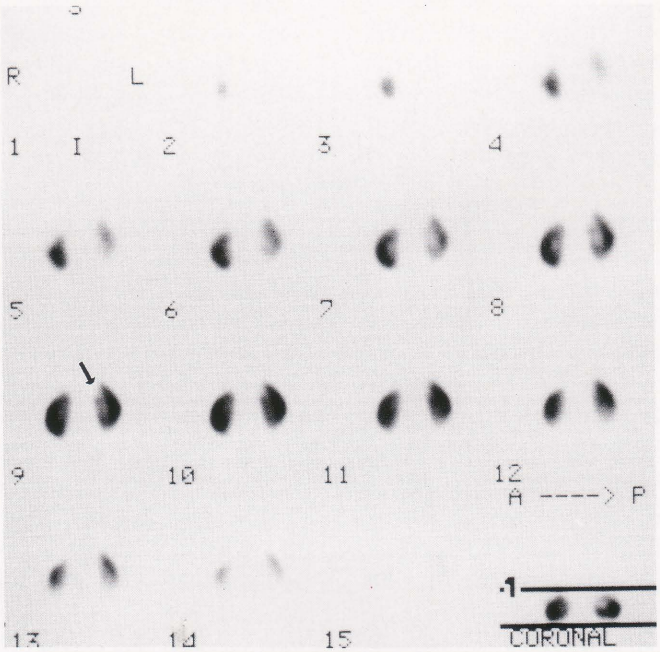
One hundred and thirty children were enrolled into this study and 14 had only one kidney, giving a total of 246 kidneys studied. The patients (Table 1) ranged in age from one month to 14 years (median, 5 years) and the male to female ratio was 1.2 : 1. A total of 473 renal scars were identified.

The sensitivity and numbers of renal scars detected by the different methods are given in Table 2. The ^{99m}Tc-DMSA SPECT-1 scan identified most scars and ultrasonography fewest. Only ten scars were missed by

A



B



C

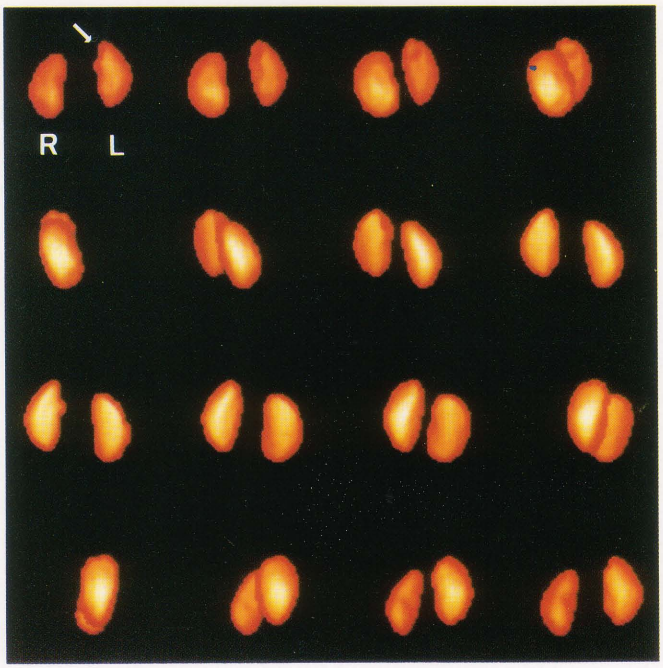


Fig. 1 ^{99m}Tc-DMSA renal scans (planar, SPECT-1, and SPECT-2) for detection of renal scarring. Figure 1A shows a false negative diagnosis in the renal planar scan. This scar is clearly demonstrated in both the SPECT-1 scan (Fig. 1B, arrow) and the SPECT-2 scan (Fig. 1C, arrow).

the ^{99m}Tc-DMSA SPECT-1, but these were detected by ^{99m}Tc-DMSA SPECT-2 and IVU. These ten defects were in ten different patients. Although the effectiveness in scar recognition of the ^{99sm}Tc-DMSA SPECT-2 renal scan is equal to or slightly less than that of the ^{99m}Tc-DMSA SPECT-1 renal scan, SPECT-2 can provide the best stereotactic localization and imaging quality among these methods (Figs. 1A, 1B, and 1C).

The results of these studies were reviewed again one week later by these radiologists and nuclear physicians. Seventeen false positives were detected, which proved to be congenital renal cysts. There were no clear correlations between the type of patient or lesion and the findings by the different scintigraphic methods. The intraobserver reliabilities for ^{99m}Tc-DMSA renal scans (planar, SPECT-1, SPECT-2), IVU, and ultrasonography were 96%, 94%, 94%, 92%, and 88%, respectively. The interobserver reliabilities for ^{99m}Tc-DMSA renal scans (planar, SPECT-1, SPECT-2), IVU, and ultrasonography were 88%, 90%, 92%, 95%, and 81%, respectively.

DISCUSSION

Although the etiology of renal scarring is still not clear, the association with UTI and vesicoureteral reflux and renal scarring is widely recognized.[2–4] Although in our studies only 42 patients (32.3%) had a UTI during the examination, when we traced the history of all the children, there were 87 (67%) who had previous UTIs. Also, 21 children (57%) had vesicoureteral reflux and 24 (47%) had unilateral or bilateral small kidneys. These results are very similar to those of Dwoskin et al.[21] and Smellie et al.[22]

For many years, IVU was considered to be the best method to use diagnosing renal scar. However, the quality of IVU images in children is not always optimal because of overlying ribs or bowel gas. Besides, such problems as allergic reactions to contrast medium in some patients and the kidney concentration power for contrast medium in children younger than two years old still have to be solved. Although tomography can help to overcome some deficiencies in image quality, the higher doses of radiation involved are unjustified for children, because of the proximity of the gonads and their increased radiosensitivity before puberty. Ultrasonography is most satisfactory both for physicians and patients because it is not invasive and uses nonionizing radiation. It can provide reliable information about the size and shape of the kidney and is accurate in diagnosing nephrocalcinosis and renal cysts.[23,24] However, our results demonstrated that its ability to detect renal scarring, especially small defects, is not satisfactory.

Recently, the ^{99m}Tc-DMSA renal scan has replaced IVU in detecting renal scarring.[5–8] The diagnostic radiopharmaceutical ^{99m}Tc-DMSA exhibits superior imaging characteristics to other radiopharmaceuticals for the clinical assessment of kidney morphology. The absolute uptake via glomerular filtration and peritubular capillary uptake following administration of the compound has been used to evaluate renal function.[25] Although a number of factors such as the chemical formulation,[26] binding to plasma macromolecules,[27] biochemical and physiological alterations and the presence of unlabeled DMSA[28] can alter the uptake, biodistribution and excretion of DMSA, most of these flaws can be overcome by strictly following the manufacturer's instructions during preparation of the commercial kit. Because DMSA can offer a biologic sense of kidney function, it can demonstrate functional damage, whereas IVU and ultrasonography can only exhibit anatomical damage which is the end result of functional disturbance.

With advances in nuclear medicine instrumentation, the resolution of scintigraphic images has improved much in the last ten years. All over the world SPECT is now a very common and popular procedure. The ^{99m}Tc-DMSA renal SPECT kidney uptake ratio and its functional volume determination have been studied,[29,30] but the role of SPECT in detecting renal cortical defects has seldom been reported.[30,31] Mouratidis et al.[18] used ^{99m}Tc-DMSA renal SPECT-1 and high-resolution planar scintigraphy to compare their sensitivity and specificity in detecting renal cortical defects in children. Although they found four defects detected by SPECT-1 (out of a total of 24) not revealed by planar scintigraphy, there was no statistically significant difference between these two methods. In our studies there were 14 scars detected by SPECT-1 (out of a total of 473), which were not observed by planar scintigraphy and this shows a significant difference ($P < 0.05$) between ^{99m}Tc-DMSA renal SPECT-1 and planar scintigraphy. The difference between the study by Mouratidis et al.[18] and this study in results may be due to more subjects being included in the present work (130 vs. 41) and different collimators used in these two examinations (low-energy, general purpose collimator vs. high-resolution collimator). Theoretically, the assessment of dynamically displayed SPECT studies (SPECT-2) allows tracing of areas of decreased activity simultaneously in three views and therefore may allow better recognition of the sites of photopenia, for example differentiation of renal medulla tissues from focal lesions, even in small scars. However, we used a low-energy, general purpose one-headed SPECT system with dynamic SPECT display software supplied by the manufacturer and recognized some deeply seated lesions with the SPECT-2 method extending into the medulla even though uptake is lower there. Although the SPECT-2 method provides the best imaging quality and stereotactic localization among these examinations, we believe that with a high-resolution triple-headed SPECT system and improved dynamic SPECT display software, we can achieve better even results. However, a small cortical abnormality detected by a planar DMSA scan during an acute episode of UTI may resolve and further work is required to ascertain

clinical significance of such findings.

In conclusion, we show that ^{99m}Tc-DMSA renal SPECT-1 studies are superior to IVU, sonography, ^{99m}Tc-DMSA renal planar and SPECT-2 studies in detecting renal scarring. SPECT is a very common and popular procedure and dynamic SPECT display software is included in most currently available computer software systems, so, it is not difficult to perform ^{99m}Tc-DMSA renal SPECT-1 and SPECT-2 scintigraphy for a given patient in many nuclear medicine departments. Although much time is necessary for data acquisition and thus may limit its utilization, we still believe that the role of SPECT-2 will become increasingly important in detecting renal scarring.

ACKNOWLEDGMENT

This work was supported by grant No. NSC 83-0412-B-075-076 from the National Science Council, Taiwan. The authors thank Dr. Ren-Shyan Liu and Dr. Bing-Fu Shih of the Department of Nuclear Medicine for interpreting these data and Dr. Sinclair Wynchank for many helpful suggestions. This study was presented in part at the European Association of Nuclear Medicine, Congress 1993, Lausanne, Switzerland, October 10–14, 1993.

REFERENCES

1. Savage JM, Dillon MJ, Shah V, Barratt TM, Williams DI. Renin and blood pressure in children with renal scarring and vesicoureteral reflux. *Lancet* 2: 411–414, 1978.
2. Bernstein J, Arant BS Jr. Morphological characteristics of segmental renal scarring in vesicoureteral reflux. *J Urol* 148: 1712–1714, 1992.
3. Berg UB. Long-term followup of renal morphology and function in children with recurrent pyelonephritis. *J Urol* 148: 1715–1720, 1992.
4. Olbing H, Claesson I, Ebel KD, et al. Renal scars and parenchymal thinning in children with vesicoureteral reflux: a 5-year report of the International Reflux Study in Children (European Branch). *J Urol* 148: 1653–1656, 1992.
5. Merrick MV, Uttley WS, Wild SR. The detection of pyelonephritic scarring in children by radioisotope imaging. *Br J Radiol* 53: 544–546, 1980.
6. Shanon A, Feldman W, McDonald P, et al. Evaluation of renal scars by technetium-labeled dimercaptosuccinic acid scan, intravenous urography, and ultrasonography: A comparative study. *J Pediatr* 120: 399–403, 1992.
7. Rushton HG, Majd M, Jantausch B, Wiedermann BL, Belman AB. Renal scarring following reflux and nonreflux pyelonephritis in children: evaluation with ^{99m}technetium-dimercaptosuccinic acid scintigraphy. *J Urol* 147: 1327–1332, 1992.
8. Arant BS Jr. Medical management of mild and moderate vesicoureteral reflux: followup studies of infants and young children. A preliminary report of the Southwest Pediatric Nephrology Study Group. *J Urol* 148: 1683–1687, 1992.
9. Kangarloo H, Gold RH, Fine RN, Diament MJ, Boechat MI. Urinary tract infections in infants and children evaluated by ultrasound. *Radiology* 154: 367–373, 1985.
10. Dillon MJ, Gordon I, Shah V. ^{99m}Tc-DMSA scarring and segmental renal vein renin estimates in children with renal scarring. *Contrib Nephrol* 39: 20–27, 1984.
11. Verber IG, Studley MR, Meller ST. ^{99m}Tc-dimercaptosuccinic acid scan as the first investigation of urinary tract infections. *Arch Dis Child* 63: 1320–1325, 1988.
12. Smellie JM, Shaw PJ, Prescod NP, Bantock HM. 99mTc dimercaptosuccinic acid (DMSA) scan in patients with established radiological renal scarring. *Arch Dis Child* 63: 1315–1319, 1988.
13. Whitear P, Shaw P, Gordon I. Comparison of 99mTc dimercaptosuccinic acid scans and intravenous urography in children. *Br J Radiol* 63: 438–443, 1990.
14. Ozen HA, Basar I, Erbas B, et al. DMSA renal scanning versus urography for detecting renal scars in vesicoureteral reflux. *Eur Urol* 17: 47–50, 1990.
15. Melis K, Vandevivere J, Hoskens C, Vervaet A, Sand A, van Acker KJ. Involvement of the renal parenchyma in acute urinary tract infection: the contribution of 99mTc dimercaptosuccinic acid scan. *Eur J Pediatr* 151: 536–539, 1992.
16. Rosenberg AR, Rossleigh MA, Brydon MP, Bass SJ, Leighton DM, Farnsworth RH. Evaluation of acute urinary tract infection in children by dimercaptosuccinic acid scintigraphy: a prospective study. *J Urol* 148: 1746–1749, 1992.
17. Williams ED. Renal single photon emission tomography: should we do it? *Semin Nucl Med* 22: 112–121, 1992.
18. Mouratidis B, Ash JM, Gilday DL. Comparison of planar and SPECT ^{99m}Tc-DMSA scintigraphy for the detection of renal cortical defects in children. *Nucl Med Commun* 14: 82–86, 1993.
19. Elison BS, Taylor D, van der Wall H, et al. Comparison of DMSA scintigraphy with intravenous urography for the detection of renal scarring and its correlation with vesicoureteral reflux. *Br J Urol* 69: 294–302, 1992.
20. Monsour M, Azmy AF, MacKenzy R. Renal scarring secondary to vesicoureteric reflux: critical assessment and new grading. *Br J Urol* 60: 320–324, 1987.
21. Dwoskin JY, Perlmutter AD. Vesicoureteral reflux in children: a computerized review. *J Urol* 109: 888–890, 1973.
22. Smellie J, Edwards D, Hunter N. Vesicoureteral reflux and renal scarring. *Kidney Int* 8: S65–72, 1979.
23. Alon U, Pery M, Davidi G, Berant M. Ultrasonography in radiologic evaluation of children with urinary tract infection. *Pediatrics* 78: 58–64, 1986.
24. Johnson CE, DeBaz BP, Shurin PA, DeBartolomeo R. Renal ultrasound evaluation of urinary tract infections in children. *Pediatrics* 78: 871–878, 1986.
25. Maneval DC, D'Argenio DZ, Wolf W. A kinetic model for ^{99m}Tc-DMSA in the rat. *Eur J Nucl Med* 16: 29–34, 1990.
26. Taylor A, Lallone RL, Hagan PL. Optimal handling of dimercaptosuccinic acid for quantitative renal scanning. *J Nucl Med* 21: 1190–1193, 1980.
27. Goldraich NP, Alvarenga AR, Goldraich IH, Ramos OL, Sigulem D. Renal accumulation of Tc-99m DMSA in the artificially perfused isolated rat kidney. *J Urol* 134: 1282–1286, 1985.
28. Provoost AP, Van Aken M. The effect of DMSA loading on the renal handling of technetium-99m in rats. *Uremia Invest* 9: 147–150, 1986.

29. Murase K, Tanada S, Ishine M, Yokoyama M, Hamamoto K. Methods for measuring the renal uptake rate of ^{99m}Tc-dimercaptosuccinic acid (DMSA): a comparative study. *J Nucl Med* 6: 725–731, 1990.
30. Groshar D, Embon OM, Frenkel A, Front D. Renal function and technetium-99m-dimercaptosuccinic acid uptake in single kidney: the value of *in vivo* SPECT quantitation. *J Nucl Med* 32: 766–768, 1991.
31. Itoh K, Asano Y, Tsukamoto E, et al. Single photon emission computed tomography with ^{99m}Tc-dimercaptosuccinic acid in patients with upper urinary infection and/or vesicoureteral reflux . *Ann Nucl Med* 5: 29–34, 1991.