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Clinical approach to renal study incidental to ^{99m}Tc-MDP bone scintigraphy

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In order to investigate the feasibility of the assessment of renal function with ^{99m}Tc-MDP, we compared renographical images, renogram patterns and the glomerular filtration rate (GFR) obtained by means of a modified Gates' method and 200 MBq of ^{99m}Tc-MDP with those obtained by means of ^{99m}Tc-DTPA. Because 19 of 20 patients had malignant tumors in the genitourinary tract, there was no difference between the two tracers in identifying a parenchymal defect corresponding to renal cancer. Of eight patients with hydronephrosis, four had a defect or decreased uptake with a dilated pelvis, whereas the other four had marked radioisotope retention in the renal pelvis or the whole kidney on serial images. There was also no difference between the two tracers in identifying hydronephrosis. Of 38 paired renograms 35 showed the same renogram patterns with both tracers. Of three patients with different renogram patterns, two had hydronephrosis. In 20 patients including three patients with bone metastasis, total GFR and split GFR obtained with both tracers correlated with a correlation coefficient of $r = 0.920$ ($p < 0.001$) and $r = 0.944$ ($p < 0.001$), respectively. Excluding bone metastasis from the analysis, a linear-regression analysis showed excellent agreement between the two measurements with a correlation coefficient of $r = 0.960$ ($p < 0.001$) and $r = 0.963$ ($p < 0.001$), respectively. The linear regression equations were $Y = 1.009X - 0.111$ and $Y = 1.034X - 0.714$, respectively. In conclusion, ^{99m}Tc-MDP can be used as a supplement to evaluate renal function incidental to the survey of bone metastases in patients with malignant tumor.

Key words: ^{99m}Tc-DTPA, ^{99m}Tc-MDP, glomerular filtration rate (GFR), split GFR

INTRODUCTION

Tc-99m methylenediphosphonate (MDP) has been clinically used for skeletal imaging for many years. The most common use is a screening test for the detection of bone metastases from malignant tumors. Patients with malignant tumors in the genitourinary tract are likely to have impaired renal function. Furthermore, damage to the kidneys is caused by chemotherapy and/or radiation therapy when the kidneys are included in the radiation field. Therefore, the estimation of renal function as well as the detection of bone metastases is inevitable in these patients.

Renal function has been estimated with Tc-99m diethylenetriamine-pentaacetic acid (^{99m}Tc-DTPA)[1] or Tc-99m mercaptoacetyltriglycine (^{99m}Tc-MAG3).[2] Since these tracers are the same Tc-99m-labeling agents as ^{99m}Tc-MDP, patients should undergo both radionuclide studies on different days to estimate renal function and skeletal lesions. It is well known that information about the kidneys can be obtained from bone scintigraphy because ^{99m}Tc-MDP is excreted through the kidneys to provide adequate visualization of the urinary tract.[3–8] If one can estimate renal function incidental to bone scintigraphy, it is very favorable from the viewpoint of convenience and cost effectiveness. As one quantitative analysis of renal function, measurement of the glomerular

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Table 1 Clinical summary of 20 patients studied

No.	Age/Sex	Diagnosis	BUN (mg/dl)	Cre (mg/dl)	Bone metastasis	HYD
1	66 M	Bladder cancer	12.6	0.8	–	–
2	76 M	Bladder cancer	13.6	0.7	–	–
3	76 M	Bladder cancer	17.1	1	–	*
4	83 M	Bladder cancer	29.4	1.4	–	L (+)
5	65 F	Bladder cancer	25.5	0.7	–	–
6	66 F	Bladder cancer	19.4	1.2	–	*
7	54 M	L-renal cancer	17	0.9	–	–
8	79 M	L-renal cancer	17	0.7	–	–
9	82 M	L-renal cancer	19.7	1	–	–
10	71 F	R-renal cancer	12	0.8	–	–
11	70 M	Prostatic cancer	26.9	1.4	(+) (diffuse)	Bil (+)
12	74 M	Prostatic cancer	11.6	0.8	Multiple	R (+)
13	75 M	Prostatic cancer	20.6	0.9	(+) (diffuse)	R (+)
14	88 M	Prostatic cancer	15.1	1.1	–	–
15	51 F	L-renal pelvic cancer	8.9	0.6	–	L (+)
16	73 F	R-renal pelvic cancer	18	0.8	–	R (+)
17	81 F	L-ureteral cancer	23.1	0.8	–	L (+)
18	75 F	R-ureteral cancer	15.7	1.1	–	R (+)
19	72 F	R-ovarian cancer	18	1.3	–	–
20	84 F	L-perirenal abscess	15.9	0.6	–	–

HYD: hydronephrosis, L: left, R: right, Bil: bilateral, *: R-kidney (–)

filtration rate (GFR) is now performed in clinical practice, particularly with Gates' method.[1] Here we have hypothesized that we can evaluate renal function with Gates' method and ^{99m}Tc-MDP.

The purpose of this study was to compare the GFR obtained with ^{99m}Tc-MDP with those obtained with ^{99m}Tc-DTPA and to investigate the potential utility of ^{99m}Tc-MDP for the assessment of renal function.

MATERIALS AND METHODS

Subjects

A total of 20 adult patients (11 males, 9 females) were enrolled. Their ages ranged from 51 to 88 years (mean 73 ± 9 years). The range of blood urea nitrogen (BUN) was 8.9–29.4 mg/dl (mean 17.8 ± 5.2 mg/dl, normal 8–20 mg/dl), and the range of serum creatinine was 0.6–1.4 mg/dl (mean 0.93 ± 0.24 mg/dl, normal 0.6–1.5 mg/dl). The diagnosis was performed with a combination of ultrasonography, intravenous pyelography (IVP) and X-ray computed tomography (CT), and confirmed by histological examination. All patients excluding a patient with perirenal abscess had malignant tumors in the genitourinary tract (Table 1). All the patients underwent both radionuclide studies with ^{99m}Tc-MDP and ^{99m}Tc-DTPA to evaluate bone metastasis and renal function within one week. Two patients had a single kidney due to nephrectomy performed previously for renal cancer. All the others had two kidneys. Eight patients were diagnosed with hydronephrosis. After the radionuclide studies, 15 patients underwent a therapeutic operation, excluding four with prostatic cancer and one with perirenal abscess.

Renography with ^{99m}Tc-DTPA

The radiopharmaceutical was prepared according to the manufacturer's instructions with the kit. Counts in preinjection and postinjection syringes were measured for 60 seconds 30 cm from a scintillation camera to determine the net amounts of activity injected. All patients were well hydrated with 200 ml of water 30 minutes before the examination and placed in the supine position.

Rapid injection of 200 MBq of ^{99m}Tc-DTPA was performed from an antecubital vein. Immediately after tracer arrival within the kidneys, data acquisition was performed for 20 minutes (1 sec per frame for 80 sec and 20 sec per frame for 1120 sec) with a scintillation camera (GCA-901A, Toshiba, Tokyo, Japan) equipped with a general purpose, low energy parallel hole type collimator. A 20% energy window was centered around the 140 keV photopeak. With a 64 × 64 matrix on a computer processing system (GMS-55A, Toshiba), serial 5-second interval dynamic images and 80-second interval serial images were recorded on radiographic film.

Skeletal and Renal Imaging with ^{99m}Tc-MDP

Imaging with ^{99m}Tc-MDP was performed on another day. For comparison with ^{99m}Tc-DTPA renography, data collection and analysis were repeated under the same conditions. On completion of renography with 200 MBq of ^{99m}Tc-MDP, the remaining 540 MBq of this tracer was injected. Whole-body imaging was done 3 hours after the second injection of ^{99m}Tc-MDP (3 hour image).

Images were comparatively interpreted as to kidney size, position, tracer activity relative to soft tissue and bone uptake, uniformity of tracer distribution, degree of radioisotope retention, and pelvicocalyceal dilation as well as whole body skeleton by two experienced nuclear physicians. Visualization of the spine was done on dynamic images and 5 minute serial images. When there was any discrepancy between two observers, consensus was obtained by discussion.

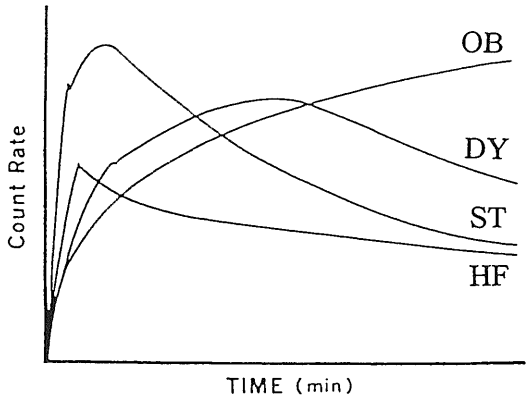

Fig. 1 Renogram patterns. ST, standard pattern; DY, delayed pattern; OB, obstructive pattern; HF, hypofunctioning pattern.

Data Analysis

A region of interest (ROI) was placed around each kidney, and a semilunar background region was placed inferior to each kidney. After background subtraction, time-activity curves (renograms) were generated for both kidneys. With a renogram of each kidney, Tmax (time from injection to time of maximum count rate), and T2/3 (time from maximum activity above the kidney to time of half/twice-maximum count rate) were obtained.

Classification of Renograms

For comparison, renogram patterns were categorized grossly into the following four patterns[9] (Fig. 1): standard pattern (ST), Tmax is less than five minutes and renal excretion is prompt; delayed pattern (DY), slow renal excretion regardless of Tmax; obstructive pattern (OB), Tmax occurs at the end of the preset time; and hypofunctioning pattern (HF), renal washout parallels the cardiac blood pool on the background.

Estimation of Total and Split GFRs

The GFR was determined by a modified Gates' method.[1] Total GFR was obtained with the percent renal uptake of ^{99m}Tc-DTPA or ^{99m}Tc-MDP in the ROIs from 2 to 3 minutes after tracer arrival within the kidneys. The following formulas were used according to the manufacturer's software.

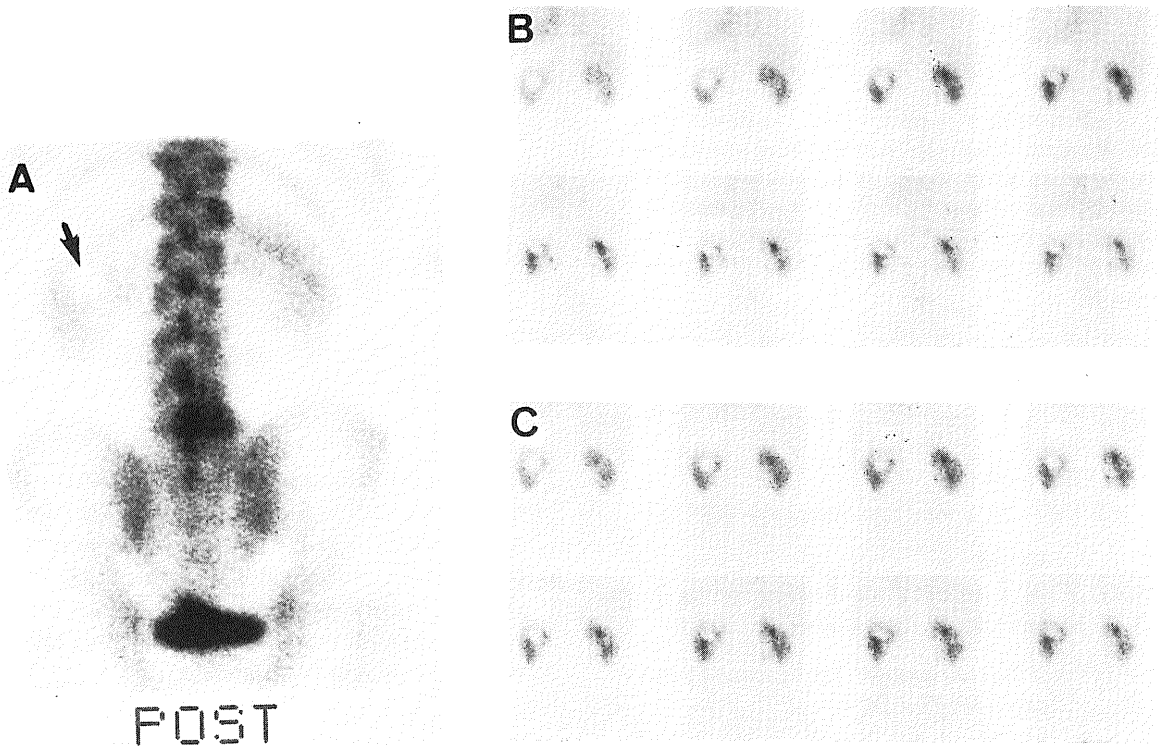

Fig. 2 Patient 8 with renal cancer in the left kidney. Images show clearly a parenchymal defect corresponding to a tumor (arrow). (A) A 3 hour image, (B) ^{99m}Tc-MDP serial images and (C) ^{99m}Tc-DTPA serial images.

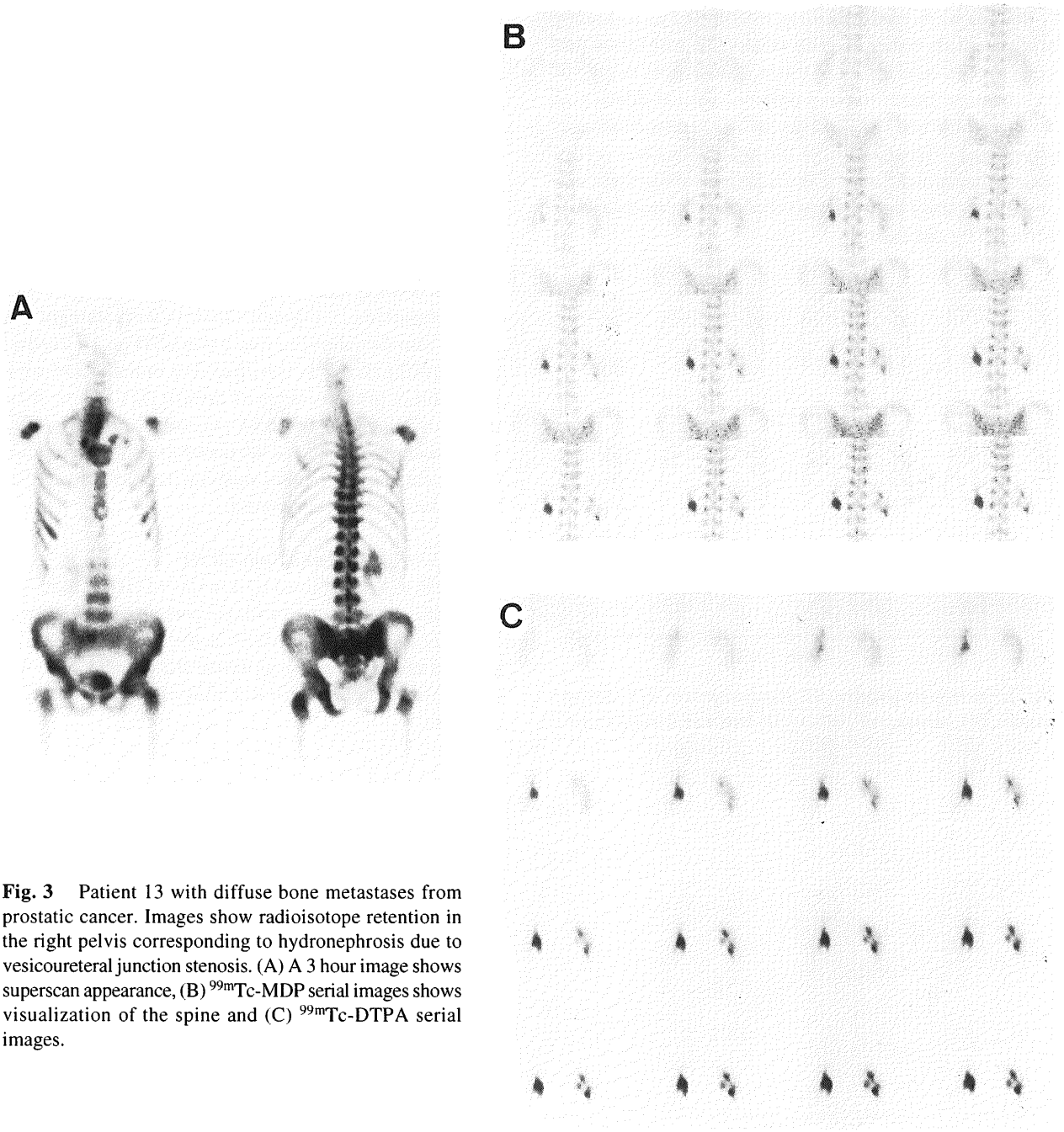

Fig. 3 Patient 13 with diffuse bone metastases from prostatic cancer. Images show radioisotope retention in the right pelvis corresponding to hydronephrosis due to vesicoureteral junction stenosis. (A) A 3 hour image shows superscan appearance, (B) ^{99m}Tc-MDP serial images shows visualization of the spine and (C) ^{99m}Tc-DTPA serial images.

Total GFR (m*l*/min)
$$= 9.75621 \times (\%\ \text{total renal uptake}) - 6.19843 \quad (1)$$

% total renal uptake
$$= (\text{L-CNT} + \text{R-CNT})/(\text{preinjection syringe counts} - \text{postinjection syringe counts}) \times 100 \quad (2)$$

$$\text{L-CNT} = (\text{left renal counts} - \text{background counts})/\exp(-0.153 \times \text{Dl}) \quad (3)$$

$$\text{R-CNT} = (\text{right renal counts} - \text{background counts})/\exp(-0.153 \times \text{Dr}) \quad (4)$$

Kidney depth was estimated from the patient's weight and height by the formulae. Dl (cm) = 13.2(W/H) + 0.7 for the left kidney, and Dr (cm) =13.3(W/H) + 0.7 for the right kidney, where W and H are the patient's weight in kg and height in cm, respectively. The value 0.153 is the linear attenuation coefficient for Tc-99m radiation in soft tissue.

The split GFR was obtained by dividing total GFR by the uptake ratio in 2–3 minutes.

Left split GFR
$$= \text{L-CNT}/(\text{L-CNT} + \text{R-CNT}) \times \text{Total GFR} \quad (5)$$

Right split GFR
$$= \text{R-CNT}/(\text{L-CNT} + \text{R-CNT}) \times \text{Total GFR} \quad (6)$$

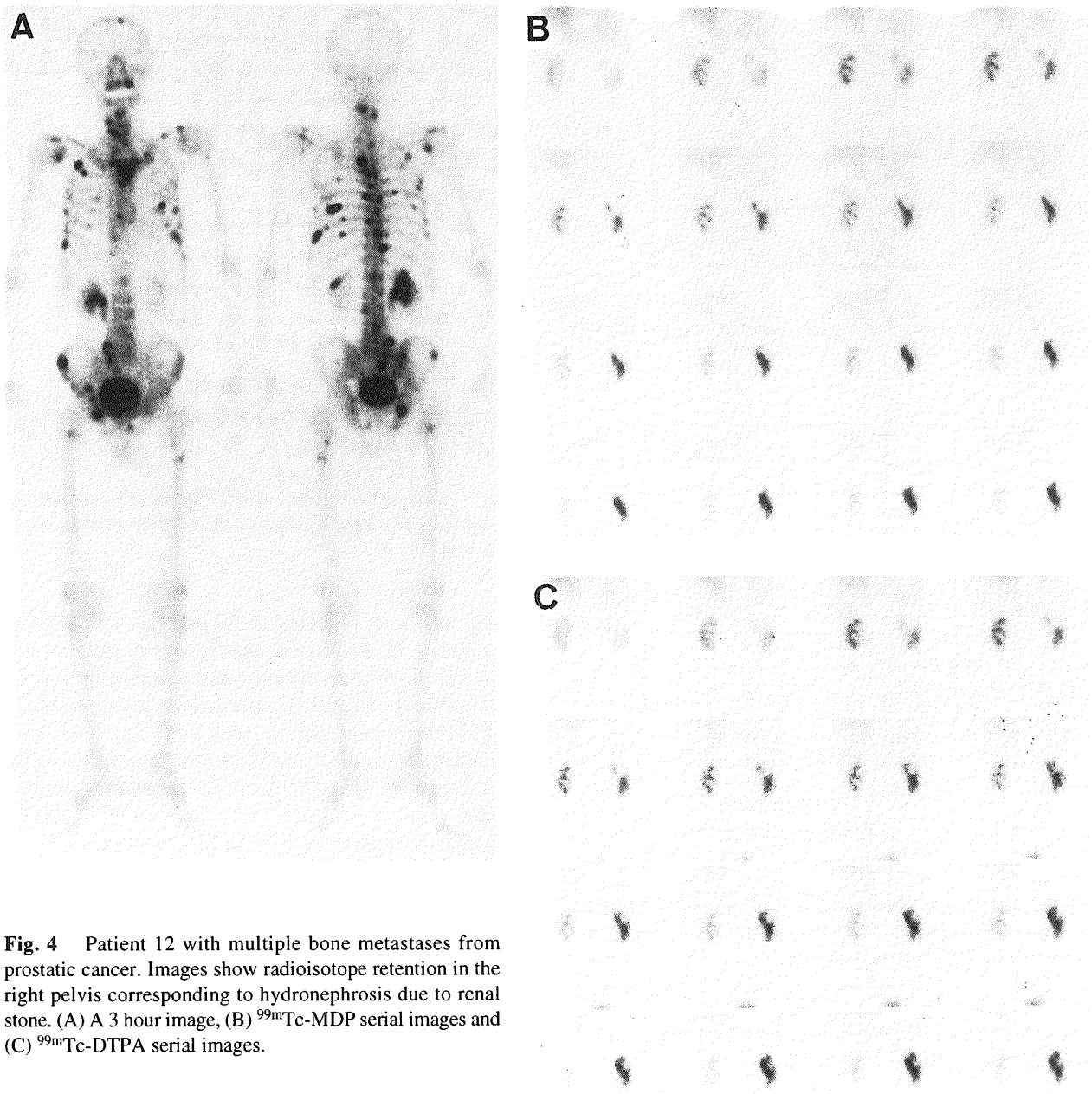

Fig. 4 Patient 12 with multiple bone metastases from prostatic cancer. Images show radioisotope retention in the right pelvis corresponding to hydronephrosis due to renal stone. (A) A 3 hour image, (B) ^{99m}Tc-MDP serial images and (C) ^{99m}Tc-DTPA serial images.

Statistical Analysis

Data were presented as the means ± S.D. Statistical analysis of GFR values obtained with ^{99m}Tc-MDP versus ^{99m}Tc-DTPA percent uptake was done by linear regression analysis. The correlation between both tracers was evaluated with Pearson's correlation coefficient. Statistical significance was defined as $p < 0.05$.

RESULTS

Identification of Renal Tumor

Both ^{99m}Tc-DTPA and ^{99m}Tc-MDP serial images in three patients clearly depicted a parenchymal defect corresponding to renal cancer. Figure 2 shows representative images in patient 8. A parenchymal defect was clearly depicted on both serial images as well as 3 hour bone scintigraphy images. The renal cancer in patient 7 was so huge (more than six cm in diameter) that both serial images showed noticeably decreased uptake in the left kidney. There was no difference between the two serial images in the identification of a parenchymal defect.

Imaging of Hydronephrosis

Of all eight patients with hydronephrosis, four showed a defect or decreased uptake with a dilated pelvis on both serial images, whereas the other four patients showed noticeable radioisotope retention in the renal pelvis or the whole kidney in the delayed phase of both serial images.

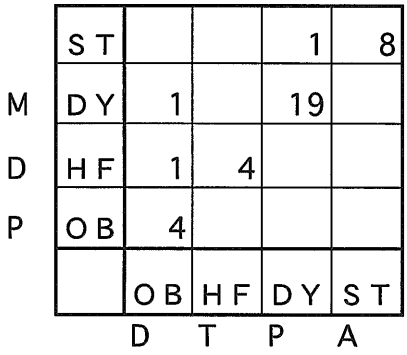

Fig. 5 Comparison of renogram patterns between the two tracers.

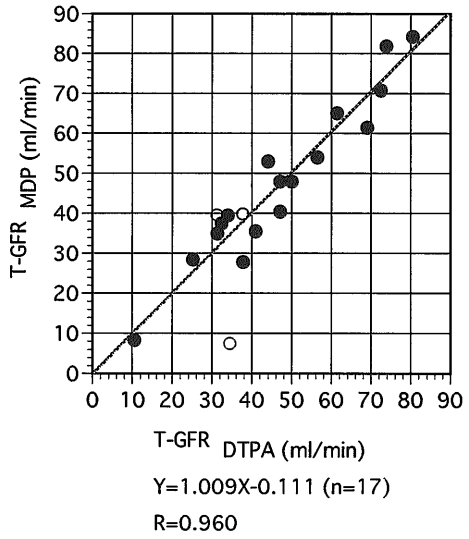

Fig. 6 Correlation between total GFRs (ml/min) obtained by means of the two tracers. (black circle; without bone metastasis, white circle; with bone metastasis)

There was no discrepancy between the two tracers in the identification of hydronephrosis.

Visualization of Spine on Images

Both dynamic images for 80 seconds after tracer arrival within the kidneys showed no visualization of the spine in a total of 20 patients. Of 17 patients without bone metastasis, both serial images for 5 minutes showed no visualization in 10, faint visualization in six, and clear visualization of the spine in one with perirenal abscess. In three patients of bone metastasis, the ^{99m}Tc-MDP serial images for 5 minutes showed clear visualization in two with diffuse bone metastasis (Fig. 3), and no visualization in one patient with multiple bone metastasis (Fig. 4), whereas ^{99m}Tc-DTPA serial images showed no visualization of the spine.

Classification of Renogram Patterns

Since two patients with a single kidney were included, 76

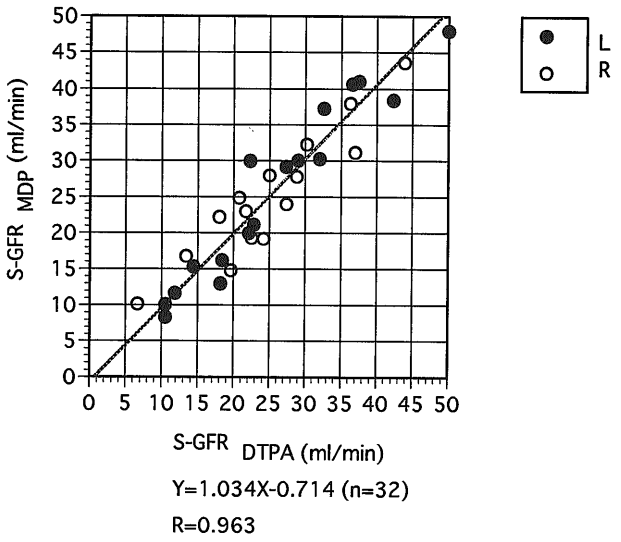

Fig. 7 Correlation between split GFRs (ml/min) obtained by means of the two tracers. (black circle; left kidney, white circle; right kidney)

renograms were obtained on 20 patients. Of 38 paired renograms, 35 showed the same renogram patterns with both tracers, whereas three showed different patterns for the two tracers (Fig. 5). Of three patients, two (patients 11 and 16) had hydronephrosis, with a different (OB) renogram pattern on the ^{99m}Tc-DTPA renogram versus an HF or DY pattern on the ^{99m}Tc-MDP renogram. Another patient (patient 14) had a DY pattern on ^{99m}Tc-DTPA versus an ST pattern on a ^{99m}Tc-MDP renogram.

Estimation of GFR

Figures 6 and 7 show the correlation between total and split GFRs obtained by means of ^{99m}Tc-DTPA and those obtained by means of ^{99m}Tc-MDP, respectively. When three patients with bone metastasis were included in the analysis, total and split GFRs obtained with ^{99m}Tc-DTPA correlated significantly with those obtained with ^{99m}Tc-MDP with a correlation coefficient of $r = 0.920$ ($p < 0.001$) and $r = 0.944$ ($p < 0.001$), respectively. The linear regression equations were $Y = 1.048X - 2.933$ and $Y = 1.051X - 1.534$, respectively. When three patients with bone metastases were excluded from the analysis, a linear-regression analysis showed excellent agreement between both tracers with a correlation coefficient of $r = 0.960$ ($p < 0.001$) and $r = 0.963$ ($p < 0.001$), respectively. The linear regression equations were $Y = 1.009X - 0.111$ and $Y = 1.034X - 0.714$, respectively.

Interpretation of 3 Hour Bone Scintigraphy Images

Ten patients were found to have normal skeletal systems. Of three with bone metastases, two had a superscan appearance on bone scintigraphy and one had multiple metastases. Seven other patients showed signs of increased uptake or small hot spots in the spine or some

joints suggesting multiple compression fracture, degenerative change or arthritis.

DISCUSSION

It is well known that renal excretion of ^{99m}Tc-labeled phosphate compounds during bone imaging provides reliable information regarding renal structure and function. Many authors have reported a number of renal abnormalities discovered incidentally on bone scintigraphy.[4–8] These abnormalities have included absent renal activity, small or displaced kidneys, urinary obstruction, focal renal parenchymal abnormalities, unilateral decrease in renal function, and asymmetric uptake. In addition, detailed views of the bladder can be obtained.[10] Since MDP is the same ^{99m}Tc-labeling agent as DTPA, the two examinations should be performed on different days. If one can simultaneously estimate renal function and skeletal lesions with ^{99m}Tc-MDP, it is valuable from the viewpoint of convenience and cost effectiveness. We, therefore, compared the GFRs obtained by means of ^{99m}Tc-MDP with those obtained by means of ^{99m}Tc-DTPA and investigated the feasibility of the assessment of renal function with ^{99m}Tc-MDP.

Detection of Parenchymal Defect on Serial Images

We compared serial images obtained with the two tracers in the identification of a parenchymal defect. Of four patients with renal cell cancer, three clearly had a parenchymal defect corresponding to a tumor, whereas the other had noticeably decreased uptake on both serial images. There was no difference between the two tracers in the identification of a parenchymal defect. Jacobson AF[7] has reported diffuse renal retention on bone scintigraphy in localized renal tumor. In such a patient careful attention should be paid to the detection of renal tumor on bone scintigraphy.

Imaging of Hydronephrosis

Of 20 patients, eight had hydronephrosis whose etiology was cancer, ureteral stone and vesicoureteral junction stenosis. Their radiographies revealed typical findings of hydronephrosis. Of eight patients, four had marked radioisotope retention in the pelvicocalyceal system, whereas the others had a defect or decreased uptake in the renal pelvis on serial images. It is noteworthy that defects and decreased uptake were observed in patients with severe dysfunction. On images there was no difference between the two tracers in the identification of hydronephrosis.

When radiography showed dilation in the pelvicocalyceal system, simple dilation must be differentiated from urinary tract obstruction. For the purpose of differentiation, diuretic radionuclide renography is helpful.[2] Although the application of diuretics to bone scintigraphy was reported to detect obstructive uropathy,[8] the discussion is beyond the scope of this paper.

Visualization of Spine on Images

Of three patients with bone metastasis, two with diffuse bone metastases had visualization of the spine on serial ^{99m}Tc-MDP images, whereas one with multiple bone metastases had no visualization of the spine. Of 17 patients without bone metastasis six had faint visualization of the spine on serial images for 5 minutes. These patients had moderate to severe dysfunction with less than 40 ml/min of total GFR. High background activity on images was also observed in patients with severe renal dysfunction.

There is a rare case in which ^{99m}Tc-DTPA serial images show visualization of the spine. Zuckier et al.[11] reported three patients of skeletal uptake in radionuclide renal perfusion studies and emphasized that the appearance of a perfused skeleton should be recognized as suggesting the presence of underlying neoplastic diseases such as leukemia, lymphoma, and multiple myeloma. In spite of our patients having malignant tumors of the kidneys, urinary bladder and prostate, serial ^{99m}Tc-DTPA images have showed no visualization of the spine. When there is approved skeletal visualization in renal perfusion studies which suggests a massive increase in perfusion to the marrow and bony matrix caused by a malignant tumor,[11] quantitative estimation of renal function based on the percent uptake of tracer may be more or less affected and be inaccurate.

Classification of Renogram Patterns

Of 38 paired renograms 35 had the same renogram patterns for both tracers. Of three patients with different patterns for the two tracers, two had hydronephrosis and one had an OB pattern on a ^{99m}Tc-DTPA renogram versus an HF pattern on a ^{99m}Tc-MDP renogram. In this patient, the count was remarkably less as a whole and the increase in the count with time was slight, although a ^{99m}Tc-DTPA renogram showed an OB pattern. The other two patients had different patterns for the two tracers. Unfortunately we cannot explain the difference between the patterns in these patients.

Estimation of GFR

To the best of our knowledge, the estimation of GFR with ^{99m}Tc-MDP has not been previously reported. Vieras et al.[12] have evaluated the usefulness of ^{99m}Tc-MDP for the assessment of renal function and reported that there was a close correlation between the early (1–3 minutes) renal uptake of ^{99m}Tc-MDP and ^{99m}Tc-DTPA ($r = 0.98$, $p < 0.001$), but they did not obtain GFR values. Concerning renograms after simultaneous injection of ^{99m}Tc-MDP and ^{111}In-DTPA, Yamashita et al.[13] reported that peak times would be a credible indicator of renal function because they were the same for both tracers. But they also did not obtain the GFR.

Many methods have been proposed to estimate the GFR with ^{99m}Tc-DTPA.[1,14] Of these methods, Gates'

method with a gamma camera is the most common. He showed that fractional renal uptake of intravenously administered ^{99m}Tc-DTPA from 2 to 3 minutes after radiotracer arrival in the kidney was proportional to the GFR. Although this method is easy to use, it is not so accurate as the blood-sampling method and contains several technical problems. These problems have included net injected activity, measurement of kidney depth, background subtraction and attenuation correction.[2,15] In comparing the GFRs obtained by means of ^{99m}Tc-MDP and ^{99m}Tc-DTPA, problems with the tracer's energy and attenuation coefficient may be regarded as the same because both tracers are the same ^{99m}Tc-labeling agents. Because the measurement of kidney depth is important for the quantitative estimation of renal function, it is desirable to estimate kidney depth by ultrasonography or the lateral view of scintigraphy in order to minimize errors. Nevertheless, we estimated kidney depth by using the formulae for simplicity. Consequently, total and split GFRs obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r = 0.960$, $r = 0.963$), respectively.

Renographies with ^{99m}Tc-MDP provide similar information concerning flow and function to those provided by renographies with ^{99m}Tc-DTPA, but the application of ^{99m}Tc-MDP to renography gives rise to significant problems because this tracer accumulates in the skeleton. As shown in this study, the GFR was underestimated in patients with bone metastases because the dose that is excreted to the kidneys decreases. A variety of patients with increased renal uptake of ^{99m}Tc-pyrophosphate have been observed in studies of urinary tract obstruction,[16] post chemotherapy,[17] metastatic calcification,[18] myoglobinuria,[19] renal artery stenosis,[20] renal vein thrombosis,[21] radiation nephritis,[22] iron overload,[23] acute tubular necrosis,[24] and administration of heparin[25] and nephrotoxic drugs.[26] It is certain that the biodistribution of ^{99m}Tc-MDP can be affected in these various conditions, but these findings of increased renal uptake were observed on 3 hour bone scintigraphy images. On the other hand, in order to obtain the GFR the percent uptake from 2 to 3 minutes after the radionuclide appearance in the kidneys is used. Although two patients with diffused bone metastasis and six with severe renal dysfunction had clear and faint visualization of the spine, respectively, on serial images for 5 minutes, in the other patients there was no visualization of the spine. It is, therefore, considered that spinal visualization has little effect on the estimation of GFR. The mechanism of renal parenchymal uptake of the ^{99m}Tc-labeled bone imaging agent is not yet fully understood and further examination is needed.

We expected to obtain information regarding renal morphology and renal function incidental to bone scintigraphy with ^{99m}Tc-MDP. If further information is of interest, more definitive renal studies should be performed with ^{99m}Tc-DTPA and ^{99m}Tc-MAG3.[14,27]

CONCLUSION

The feasibility of the assessment of renal function with ^{99m}Tc-MDP was confirmed in patients without remarkable skeletal abnormality. It can be performed incidental to bone scintigraphy and is expected to provide useful information in monitoring renal function.

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REFERENCES

1. Gates GF. Split renal function testing using ^{99m}Tc-DTPA: a rapid technique for determining differential glomerular filtration. *Clin Nucl Med* 1983; 8: 400–407.
2. Taylor A. Radionuclide renography: a personal approach. *Semin Nucl Med* 1999; 29: 102–127.
3. Glass EC, DeNardo GL, Hines HH. Immediate renal imaging and renography with ^{99m}Tc methylene diphosphonate to assess renal blood flow, excretory function, and anatomy. *Radiology* 1980; 135: 187–190.
4. Adams KJ, Shuler SE, Witherspoon LR, Neely HR. A retrospective analysis of renal abnormalities detected on bone scans. *Clin Nucl Med* 1980; 5: 1–7.
5. Koizumi K, Tonami N, Hisada K. Diffusely increased Tc-99m-MDP uptake in both kidneys. *Clin Nucl Med* 1981; 6: 362–365.
6. Chayes ZW, Strashun AM. Improved renal screening on bone scans. *Clin Nucl Med* 1980; 5: 94–97.
7. Jacobson AF. Diffuse renal retention on bone scintigraphy in localized clear-cell renal epithelial neoplasm. *J Nucl Med* 1995; 36: 817–819.
8. Haden HT, Katz PG, Konerding KF. Detection of obstructive uropathy by bone scintigraphy. *J Nucl Med* 1988; 29: 1781–1785.
9. Itoh K, Tsukamoto E, Nagao K, Nakada K, Kanegae K, Furudate M. Captopril renography with Tc-99m DTPA in patients with suspected renovascular hypertension prospective and retrospective evaluation. *Clin Nucl Med* 1993; 18: 463–471.
10. Bilchik TR, Spencer RP. Bladder variants noted on bone and renal imaging. *Clin Nucl Med* 1993; 18: 60–67.
11. Zuckier LS, Weissmann HS, Kaplun L, Schlossberg I, Gade MF, Freeman LM. Significance of skeletal uptake detected on radionuclide renal perfusion studies. *Clin Nucl Med* 1987; 12: 448–452.
12. Vieras F, Achong DM, Tulchinsky M, Smith JJ. Quantitation of differential renal function with Tc-99m MDP. *Clin Nucl Med* 1991; 16: 649–651.
13. Yamashita M, Miyazaki T, Imahori Y, Ohmori Y, Oka T, Murakami K. Renogram study using ^{99m}Tc-methylene-diphosphonate. *Radioisotopes* 1985; 34: 382–385.
14. Russell CD, Bischoff PG, Konzen F, Rowell KL, Yester MV, Lloyd LK, et al. Measurement of glomerular filtration rate using ^{99m}Tc-DTPA and the gamma camera: a comparison of methods. *Eur J Nucl Med* 1985; 10: 519–521.
15. Awdeh M, Kouris K, Hassan IM, Abdel Dayem HM.

Factors affecting the Gates' measurement of glomerular filtration rate. *Am J Physiol Imag* 1990; 5: 36–41.
16. Siddiqui AR. Increased uptake of technetium-99m-labeled bone imaging agents in kidneys. *Semin Nucl Med* 1982; 12: 101–102.
17. Lutrin CL, McDougall IR, Goris ML. Intense concentration of Tc-99m-pyrophosphate in the kidneys of children treated with chemotherapeutic drugs for malignant disease. *Radiology* 1978; 128: 165–167.
18. Arbona GL, Antonmattei S, Tetalman MR, Scheu JD. Tc-99m-diphosphonate distribution in a patient with hypercalcemia and metastatic calcifications. *Clin Nucl Med* 1980; 5: 422.
19. Sheth KJ, Sty JR, Johnson F, Tisdale P. Myoglobinuria with acute renal failure and hot kidneys seen on bone imaging. *Clin Nucl Med* 1984; 9: 498–501.
20. Lantieri RL, Lin MS, Martin W, Goodwin DA. Increased renal accumulation of Tc-99m-MDP in renal artery stenosis. *Clin Nucl Med* 1980; 5: 305–309.
21. Lamki LM, Wyatt JK. Renal vein thrombosis as a cause of excess renal accumulation of bone seeking agents. *Clin Nucl Med* 1983; 8: 267–268.
22. Titelbaum DS, Fowble BF, Powe JF, Martinez FJ. Renal uptake of technetium-99m methylene diphosphonate following therapeutic radiation for vertebral metastases. *J Nucl Med* 1989; 30: 1113–1116.
23. Choy D, Murray PC, Hoschl R. The effect of iron on the biodistribution of bone scanning agents in humans. *Radiology* 1981; 140: 197–202.
24. Watanabe N, Shimizu M, Kageyama M, Kamei T, Seto H, Kakishita M. Diffuse increased renal uptake on bone scintigraphy in acute renal tubular necrosis. *Clin Nucl Med* 1993; 19: 19–21.
25. Challa S, Miller JF. Extraskeletal uptake of technetium-99m-MDP in sites of heparin administration. *J Nucl Med* 1998; 39: 893–895.
26. Bernard MS, Hayward M, Hayward C, Mundy L. Evaluation of intense renal parenchymal activity ("hot kidneys") on bone scintigraphy. *Clin Nucl Med* 1990; 15: 254–256.
27. Taylor A, Corrigan P, Galt J, Garcia EV, Forks R, Jones M, et al. Measuring Tc-99m MAG3 clearance with an improved camera based method. *J Nucl Med* 1995; 36: 1689–1695.