Annals of Nuclear Medicine Vol. 18, No. 5, 419–425, 2004

Assessment of the optimal time interval and background region of interest in the measurement of differential renal function in Tc-99m-EC renography

A. Fuat Yapar,* Mehmet Aydin,* Mehmet Reyhan,* Zeynep Yapar** and Nazli Altun Yologlu*

*Department of Nuclear Medicine, Baskent University Adana Teaching and Research Center, and
**Department of Nuclear Medicine, Cukurova University Faculty of Medicine, Adana, Turkey

Background: Differential renal function (DRF) measurements are routinely corrected for background, which mainly affects the reproducibility and accuracy of the measurement. The present study was conducted to identify the most appropriate background ROI and optimal time interval in the calculation of DRF for EC renography. ***Materials and Methods:*** Nineteen patients were studied. For determination of DRF in EC renography, the selected time intervals were 0.5–1.5; 0.5–2; 1–2; 1.5–2.5; 2–3 min, and the background ROI types were inferolateral crescent, lateral crescent, and perirenal shaped. The reference DRF was obtained through DMSA study. For low functioning kidney of each patient, relative uptake differences between the DMSA and EC scans were calculated. Then, the mean differences and the standard deviations were found. ***Results:*** The highest correlation was between the DRF values obtained using inferolateral background ROI in 0.5–2 minutes of EC scintigraphy and the DRF values obtained through posterior DMSA images ($r = 0.9889$). However, there were no statistically significant differences between the mean DRF values obtained for each time interval with each ROI type ($p > 0.05$). For all the time intervals and background ROIs, the mean of the differences was <0.9%. In conclusion, in obtaining comparable DRF values from EC and DMSA studies, none of the background types proved superior. Also our research for optimal time interval showed that EC scintigraphy underestimates the DRF when compared to DRF obtained from DMSA study. The DRF has a tendency to decrease as the later time intervals are used. The time intervals less than 2.5 minutes show lower underestimation of DRF values.

Key words: differential renal function, renal scintigraphy, Tc-99m-EC

INTRODUCTION

Tc-99m-ethylene dicysteine (Tc-99m-EC) is a newly developed renal tubular agent that can be labeled with technetium. The clearance of Tc-99m-EC is found to be similar to the clearance of orthoiodohippurate (OIH) in both healthy volunteers and in patients with renal disorders,[1–4] and can be used as an index of renal function. Compared to OIH, EC offers the advantages of high-quality images and low radiation dose to the patient. Easy labeling, high radiochemical purity, and long term stability may also be considered as other advantages.

One of the most important parameters that can be derived from dynamic renal scintigraphy is measurement of differential renal function (DRF).[5] Individual kidney function influences the clinical judgment with regard to assessment of therapy and will affect the decision on whether to perform nephrectomy. Commercially available software programs can be used to measure the renal functions at different time intervals, 1–2 or 1–2.5 or 2–3 min, after radiopharmaceutical injection. The reproducibility of the results is the most important aspect from the clinical point of view since it allows a longitudinal study

Received January 8, 2004, revision accepted March 31, 2004.
For reprint contact: A. Fuat Yapar, M.D., Baskent Universitesi, Adana Uygulama ve Arastirma Merkezi, Nukleer Tip Bl. Dadaloglu Mah., 01250 Yuregir-Adana, TURKEY.
E-mail: fyapar@dr.com
fyapar@veezy.com

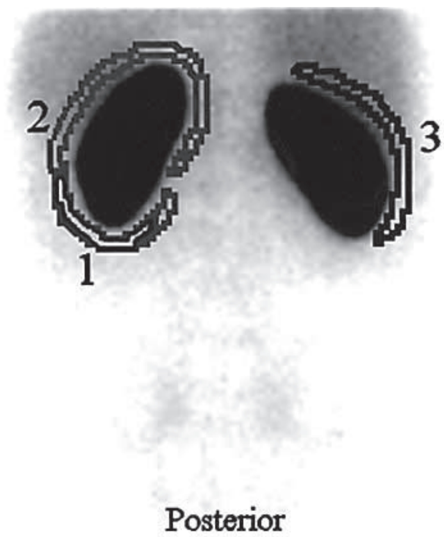

Fig. 1 Background ROIs in Tc-99m-EC scintigraphy. (1) inferolateral, (2) perirenal and (3) lateral ROI.

in patients to evaluate whether there is a significant change in renal function. The DRF measurements are routinely corrected for background, which mainly affects the reproducibility and accuracy of the measurement.

The most appropriate region of interest (ROI) for background in OIH renograms has been shown to be between the kidneys.[6] In DTPA renography, the perirenal ROI was found to be superior to subrenal or suprarenal ROI for background correction.[7] In another study performed with MAG3, no significant difference was found between the lateral and perirenal ROIs, but the need for background correction was pointed out.[8] According to our review of the literature, there are no data regarding the type of background ROI in EC renography.

The present study was conducted to identify the most appropriate background ROI and optimal time interval in the calculation of DRF for EC renography. For this purpose, EC renography was performed on a group of patients, and the DRF was calculated several times for each determined background ROI and time interval. Then, the DRF values obtained from EC scans using different variables were compared with those obtained from DMSA scanning as references.

MATERIALS AND METHODS

Subjects

Nineteen patients (13 F, 6 M; age range: 0.2–60 yrs; mean age: 14.4 ± 19 yrs) were studied. All the patients underwent both EC and DMSA scintigraphies in the same week, with the second study performed at least 2 days after the first one.

Tc-99m-EC scintigraphy

The adults were orally hydrated with 500–1000 m*l* water 60 min before the study. In the babies and young children, normal saline solution was administered intravenously at a rate of 15 m*l*/kg over a 30 min period, beginning at least 15 min before renography. Following intravenous bolus of 37–296 MBq (1–8 mCi) Tc-99m-EC (Institute of Isotopes, Hungary), images were acquired posteriorly at 1 sec/frame for 60 frames, 5 sec/frames for 24 frames and 30 sec/frame for 34 frames with patients in the supine position. Data were acquired using a gamma camera (Siemens E-cam, USA) equipped with a low energy, all-purpose, parallel-hole (LEAP) collimator, and the photo peak was selected at 140 keV with a 20% window.

Tc-99m-DMSA scintigraphy

As in the EC study, scintigraphy was performed with the patient in the supine position. Anterior and posterior images were acquired 4 h after the injection of 37–111 MBq (1–3 mCi) Tc-99m-DMSA using a dual head gamma camera (Siemens E-cam, USA) equipped with LEAP collimator.

Differential renal function calculation in EC study

For determination of DRF in EC renography, the selected time intervals were 0.5–1.5; 0.5–2; 1–2; 1.5–2.5; 2–3 min, and the background ROI types were inferolateral crescent (IL), lateral crescent (L), and perirenal (P) shaped (Fig. 1). All of the studies were independently processed by two observers for all the time intervals using the same kidney and background ROIs. DRF calculation was based on the integral method with and without renal depth correction, and for this calculation; all types of background ROIs were used for each time interval. To achieve renal depth correction, for the adults, Taylor formula[9] and for the children, Lythgoe formula[10] were used. The reference DRF was obtained through DMSA study.

Differential renal function calculation in DMSA study

Regions of interest around each kidney and 3 background ROIs (inferolateral, lateral and perirenal) were defined on the anterior and posterior images. Counts within these regions (kidneys and a mean of 3 background ROIs) were used to calculate the background corrected counts from each kidney. The relative renal function (RRF) of the right kidney (RKF) was calculated from the posterior counts using

$$\mathrm{RKF}_{(\mathrm{POST})} = \frac{C_{R(\mathrm{POST})}}{C_{R(\mathrm{POST})} + C_{L(\mathrm{POST})}} \times 100\%$$

where $C_{R(\mathrm{POST})}$ and $C_{L(\mathrm{POST})}$ are the background corrected counts of the right and the left kidneys respectively in the posterior view. The calculation was also performed using the geometric mean (GM) of the counts of the anterior and the posterior views so that the relative renal function of the right kidney was given by

$$\mathrm{RKF}_{(\mathrm{GM})} = \frac{\sqrt{C_{R(\mathrm{POST})} \times C_{R(\mathrm{ANT})}}}{\sqrt{C_{R(\mathrm{POST})} \times C_{R(\mathrm{ANT})}} + \sqrt{C_{L(\mathrm{POST})} \times C_{L(\mathrm{ANT})}}} \times 100\%$$

where $C_{R(\mathrm{ANT})}$ and $C_{L(\mathrm{ANT})}$ are the background corrected counts of the right and the left kidneys in the anterior view.

The DRF values calculated through posterior DMSA images only and the DRF values obtained without depth correction in EC scintigraphy were compared, while the DRF values obtained by the use of geometric mean were compared with the DRF values with depth correction in EC scintigraphy. With relative DMSA uptake as the reference method, we compared this percentage with the corresponding EC relative uptake. For the low functioning kidney of each patient, differences between the DMSA and EC relative uptakes were calculated, taking into account the negative or positive sign of this difference. Then, the mean differences, absolute mean differences, and the standard deviations were calculated.[11] The standard deviation of these differences represented the precision of the technique.

Statistical analysis

The difference between DMSA and EC relative uptake for the kidney with the lowest uptake was calculated for each patient, taking into account the negative or positive sign of the difference. The mean differences represented the systematic bias between the two measurements. A negative value means that the EC relative uptake is systematically overestimated compared to the DMSA relative uptake, whereas a positive value means that the EC uptake is underestimated. The standard deviation of these differences represents the accuracy of the technique.[11] Simple linear regression analysis was applied to determine the correlation coefficients and a repeated measures analysis of variance was used to determine whether there was a difference between the background ROI options for each time interval.

RESULTS

The DRF values calculated for all the time intervals using three ROI types were significantly correlated with the DRF values obtained through DMSA scintigraphy (r values > 0.95). The highest correlation was between the DRF values obtained using IL background ROI in 0.5–2 minutes of EC scintigraphy and the DRF values obtained through posterior DMSA images ($r = 0.9889$) (Figs. 2 and 3). However, there were no statistically significant differences between the mean DRF values obtained for each time interval with each ROI type ($p > 0.05$). No systematic bias among the methods was observed for the mean of the differences between EC and DMSA relative uptake. For all the time intervals and background ROIs, the mean of

Table 1 The means, absolute means and standard deviations (SD) of differences between the DRF values obtained Tc-99m-DMSA and Tc-99m-EC scintigraphy

		GM differences*		Absolute GM differences**		POST differences#		Absolute POST differences##	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
0.5–1.5 min	Inferolateral	0.131	3.382	2.552	2.140	0.184	2.714	2.394	1.161
	Lateral	0.289	3.437	2.657	2.108	0.342	2.068	1.552	1.363
	Perirenal	0.394	3.490	2.605	2.276	0.447	2.565	1.921	1.701
0.5–2 min	Inferolateral	0.184	3.158	2.342	2.055	0.236	2.394	2.026	1.207
	Lateral	0.447	3.475	2.710	2.129	0.5	2.533	1.815	1.788
	Perirenal	0.710	3.296	2.605	2.058	0.763	2.780	1.921	2.109
1–2 min	Inferolateral	0.447	3.261	2.605	1.919	0.5	2.651	2.078	1.652
	Lateral	0.657	3.535	2.710	2.281	0.710	2.567	1.868	1.854
	Perirenal	0.658	3.325	2.605	2.085	0.710	2.683	1.815	2.062
1.5–2.5 min	Inferolateral	0.447	3.059	2.394	1.875	0.5	2.488	1.815	1.725
	Lateral	0.763	3.384	2.710	2.077	0.815	2.410	1.868	1.681
	Perirenal	0.657	3.350	2.710	1.981	0.710	2.534	1.973	1.687
2–3 min	Inferolateral	0.5	3.304	2.552	2.074	0.552	2.597	2.026	1.653
	Lateral	0.868	3.628	2.921	2.225	0.921	2.572	2.184	1.574
	Perirenal	0.815	3.420	2.763	2.084	0.868	2.448	2.026	1.567

* differences between DRF values for the kidney with lowest uptake obtained by geometric mean of Tc-99m-DMSA images and Tc-99m-EC images with depth correction.

** absolute differences between DRF values for the kidney with lowest uptake obtained by geometric mean of Tc-99m-DMSA images and Tc-99m-EC images with depth correction.

\# differences between DRF values for the kidney with lowest uptake obtained by posterior Tc-99m-DMSA images and Tc-99m-EC images without depth correction.

\#\# absolute differences between DRF values for the kidney with lowest uptake obtained by posterior Tc-99m-DMSA images and Tc-99m-EC images without depth correction.

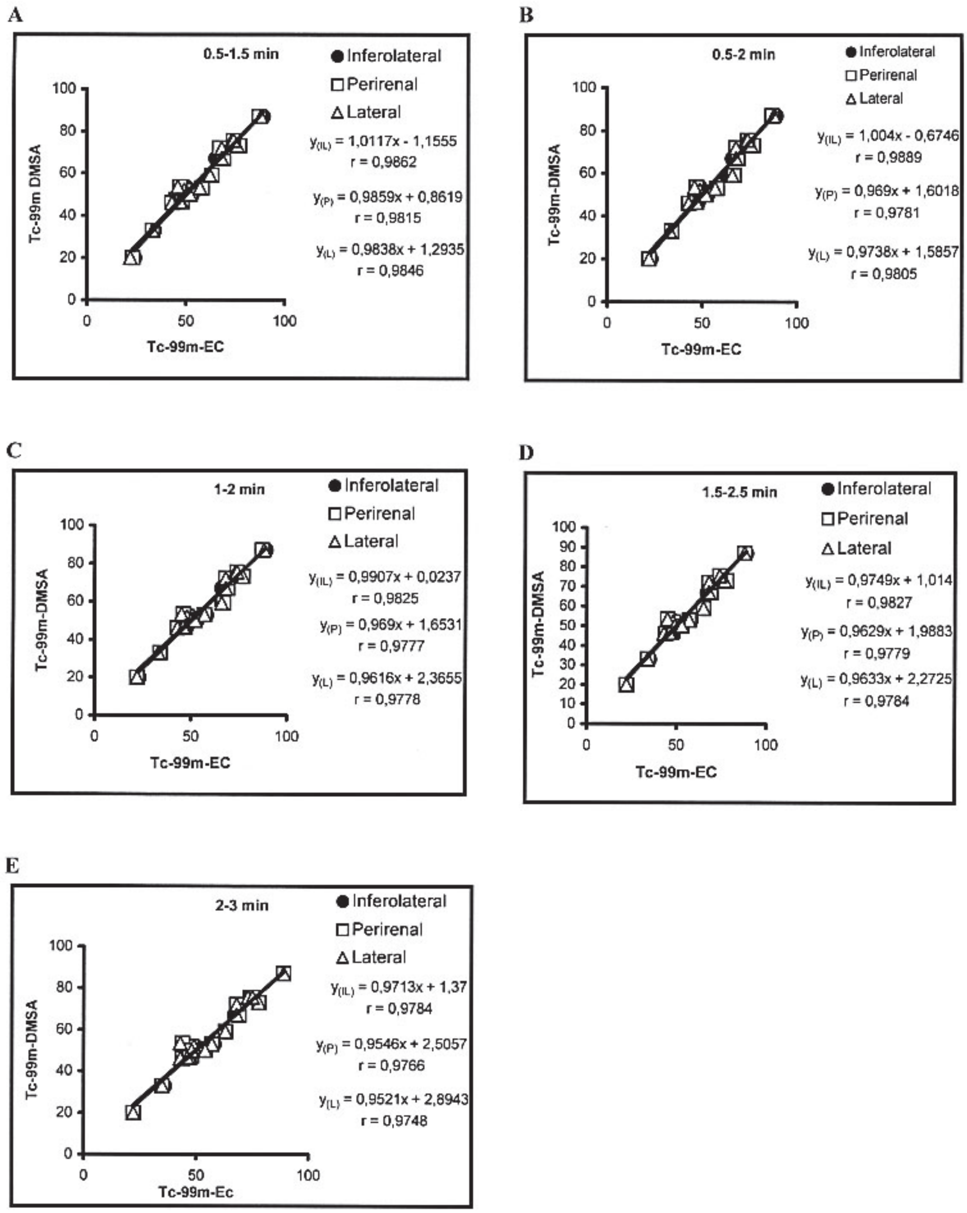

Fig. 2 Plots of the right kidney DRF values obtained by posterior Tc-99m-DMSA images versus Tc-99m-EC images without depth correction at different time intervals: (A) 0.5–1.5 min, (B) 0.5–2 min, (C) 1–2 min, (D) 1.5–2.5 min and (E) 2–3 min.

the differences was <0.9%. EC scintigraphy of each interval and backround ROI type was found to underestimate the DRF values by 0.1% to 0.8% for the values based on geometric means and 0.1% to 0.9% for the values based on posterior DMSA images (Table 1). The lowest absolute mean difference (AMD) in EC scintigraphy was between the DRF values obtained through posterior DMSA images and the DRF values obtained in 0.5–1.5 minutes using L background ROI (AMD = 1.5%). The lowest AMD value for the DRF values based on geometric means was the value calculated for 0.5–2 min interval with IL background ROI use (AMD = 2.3%). When compared with the DRF values calculated through geometric means, the highest accuracy rate (1.87%) was for 1.5–2.5 min interval with IL background ROI. When compared with the DRF values calculated by using DMSA images only, the highest accuracy value (1.16%) was for 0.5–1.5 min interval with IL background ROI use.

The two observers who marked the kidney and background areas used in DRF calculations were largely in agreement; thus, no significant interobserver variability was detected (r = 0.991).

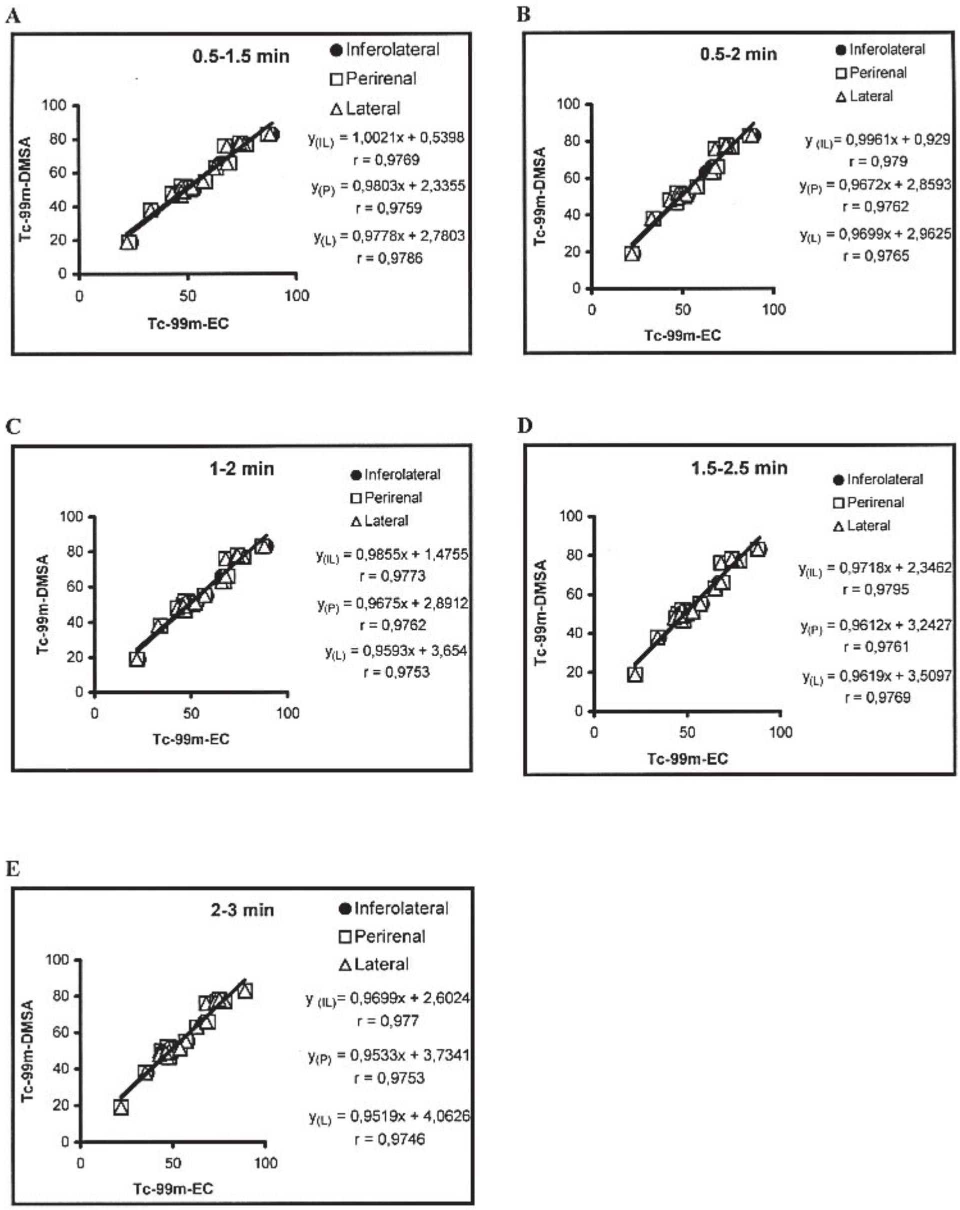

Fig. 3 Plots of the right kidney DRF values obtained by geometric mean of anterior and posterior Tc-99m-DMSA images versus Tc-99m-EC images with depth correction at different time intervals: (A) 0.5–1.5 min, (B) 0.5–2 min, (C) 1–2 min, (D) 1.5–2.5 min and (E) 2–3 min.

DISCUSSION

Quantitative assessment of relative (differential) individual renal function is a major role of radionuclide renography. Individual kidney function influences the clinical judgement with regard to assessment of therapy. One of the major errors in DRF calculations results from the level of accuracy of background correction. Several organs such as the liver, spleen, adrenals, duodenum, large vessels, gut, and several tissues including the skin, muscles and fat layer are superimposed on the renal background. The compatibility of the radiopharmaceutical choice with the organ and tissue involvement with background ROI is directly related to the accuracy of background correction. In our study, there were no significant differences among the calculated differential functions for each background ROI type in Tc-99m-EC scintigraphy. The literature reveals various types of background areas including the hepatic, perirenal, interrenal, subrenal areas and the heart recommended for OIH, DTPA and MAG3 radionuclide renography.[12–23] DTPA is a glomerular agent, with slower clearance than that of

MAG3 and EC, and with a lower extraction rate.[2,18,19] Therefore, its prolonged existence in the vascular bed increases the vascular activity. Peters et al.[7] have shown perirenal ROI to be superior to subrenal and suprarenal ROI for DTPA. Accordingly, perirenal background ROI has proven superior because it contains both suprarenal background ROI, which regulates intravascular background activity (intrahepatic and intrasplenic) and infrarenal background ROI, which regulates interstitial background activity. Gates compared inferolateral and ring background corrections and reported slightly better results for the inferolateral background although the differences were not significant.[20]

Tondeur et al.[21] calculated MAG3 clearance through gamma camera method and showed that both the right and left renal clearances were higher with suprarenal background ROI use than with perirenal and subrenal background ROI use. Furthermore, in the study of Inoue et al.,[22] perirenal background ROI was slightly more correlated than subrenal background ROI. Taylor et al.[8] concluded that when no background correction was performed or no inferior background ROI was used, DRF values were significantly underestimated compared to lateral and automated perirenal ROI, and there was minimal error in perirenal ROI use.

Tc-99m-EC has recently been introduced as an alternative to OIH and Tc-99m-MAG3 for renal imaging and evaluation of renal function. Despite having similar image quality to that of Tc-99m-MAG3, its hepatic uptake is lower than that of MAG3,[23,24] and its clearance and renal extraction rates are higher than those of MAG3.[3] Moreover, its plasma protein binding fraction is significantly lower than that of MAG3 and OIH.[1–3] Due to the characteristics of Tc-99m-EC, there is less body background activity in the images; thus, renal margins are more distinctive. In our study, no background ROI type was found superior to any other in Tc-99m-EC scintigraphy. For the same reasons, although no automatic or semiautomatic ROI was used, the results of the two observers were highly compatible ($r = 0.991$). Kibar et al.[25] used perirenal background ROI only and showed the DRF values calculated through DMSA and EC scintigraphy to be highly correlated. However, other background ROI types were not used. Perirenal ROI has been recommended as the most useful type in "Guidelines for standard and diuretic renogram in children" (EANM).[17] The literature, on the other hand, reveals no studies comparing various background types in Tc-99m-EC. The time interval recommended in the guidelines is within 60–120 seconds. If the tracer and diuretic are administered simultaneously, due to rapid passage of the tracer, the recommended time interval for DRF calculation is 40–100 seconds. In our study, simultaneous diuretic injection was not performed, but DRF values were calculated for 5 different time intervals (0.5–1.5; 0.5–2; 1–2; 1.5–2.5; 2–3 min). The DRF values calculated for each time interval and the DRF values calculated through DMSA scintigraphy did not have statistically significant differences. Nevertheless, the mean difference between the DRF values, particularly those obtained by inferolateral and lateral background ROI use, and the DRF values calculated through DMSA scintigraphy increased as the time interval advanced from 0.5 minutes to 3 minutes. For all the background ROI types, the most significant mean differences were within 2–3 minute time intervals. The mean parenchymal transit time index, mean whole-kidney transit time index, and mean parenchymal transit time values reported for Tc-99m-EC are less than 3 minutes.[23,26] In conformity with the literature, the DRF values were underestimated more by the values obtained in 2–3 minute time intervals.

The correlation coefficients between the DRF values calculated without depth correction in EC scintigraphy and the DRF values calculated through posterior DMSA images were higher than the correlation coefficients between the DRF values calculated after depth correction in EC scintigraphy and the DRF values calculated through the geometric means of DMSA images. This can be accounted for by the comparison of the DRF values obtained without depth correction in EC scintigraphy and the DRF values obtained through posterior DMSA images without depth correction. In other words, the correlation coefficient is high because the DRF values for both agents calculated through posterior images without depth correction were compared. However, in EC scintigraphy, DRF values calculated by the Taylor formula[9] for adults and Lythgoe formula[10] for children after depth correction were compared with the DRF values calculated through the geometric means of anterior and posterior DMSA images. Taylor and Lythgoe formulas are nomograms which are used in renal depth estimation based on the weight, height, and age parameters of the patients. The renal depths calculated are not the real but estimated renal depths. If the difference between the depths of kidneys is great, the errors in the DRF values calculated after the depth correction based on these formulas will increase. On the other hand, the DRF values calculated through the geometric means of anterior and posterior images of DMSA scintigraphy are not affected by the difference in the kidney depths.[10,27,28] Thus, the correlation coefficient between the DRF values calculated with depth correction in EC scintigraphy and the DRF values calculated through the geometric means of DMSA images has been found to be relatively lower.

To sum up, in obtaining comparable DRF values from EC and DMSA studies, none of the background types proved superior to the others. This finding was attributed to the negligible extrarenal clearance and high renal extraction of Tc-99m-EC, enough to greatly reduce the tracer amount in the spaces of interference. In addition, our research on optimal time interval showed that Tc-99m-EC scintigraphy underestimates the DRF when compared to DRF obtained from Tc-99m-DMSA study. The

DRF has a tendency to decrease as the later time intervals are used. The time intervals less than 2.5 minute show lower underestimation of DRF values.

REFERENCES

1. Van Nerom CG, Bormans GM, De Roo MJ, Verbruggen AM. First experience in healthy volunteers with technetium-99m-L,L-ethylenedicysteine, a new renal imaging agent. *Eur J Nucl Med* 1993; 20: 738–746.
2. Kabasakal L, Turoglu HT, Onsel C, Ozker K, Uslu I, Atay S, et al. Clinical comparision of Technetium-99m-EC, Technetium-99m-MAG3 and Iodine-131-OIH in renal disorders. *J Nucl Med* 1995; 36: 224–228.
3. Kabasakal L, Atay S, Vural AV, Ozker K, Sonmezoglu K, Demir M, et al. Evaluation of technetium-99m-ethylenedicysteine in renal disorders and determination of extraction ratio. *J Nucl Med* 1995; 36: 1398–1403.
4. Nielsen SS, Poulsen EU, Markversen J, Nielsen LE, Bacher T, Rehling M. Clearance and renal extraction of technetium-99m-L,L-ethylenedicysteine, I-131-orthoiodohippurate and I-125-iothalamate in pigs. *Clin Physiol* 1999; 19: 338–343.
5. Taylor A Jr, Nally JV. Clinical applications of renal scintigraphy. *Am J Roentgenol* 1995; 164: 31–41.
6. Oei HY. Dynamic and static renal imaging. In *Nuclear Medicine in Clinical Diagnosis and Treatment*, Murray IPC, Ell PJ (eds) 1st ed. New York; Churchill Livingstone, Inc., 1994: 213–227.
7. Peters AM, George P, Ballardie F, Gordon I, Todd-Pokropek A. Appropriate selection of background for ^{99m}Tc-DTPA renography. *Nucl Med Commun* 1988; 9: 973–985.
8. Taylor A Jr, Thakore K, Folks R, Halkar R, Manatunga A. Background subtraction in technetium-99m-MAG3 renography. *J Nucl Med* 1997; 38: 74–79.
9. Taylor A, Lewis C, Giacometti A, Hall EC, Barefield KP. Improved formulas for the estimation of renal depth in adults. *J Nucl Med* 1993; 34: 1766–1769.
10. Lythgoe MF, Gradwell MJ, Evans K, Gordon I. Estimation and relevance of depth correction in paediatric renal studies. *Eur J Nucl Med* 1998; 25: 115–119.
11. Piepsz A, Tondeur M, Ham H. Relative ^{99m}Tc-MAG3 renal uptake: Reproducibility and accuracy. *J Nucl Med* 1999; 40: 972–976.
12. Tamminen TE, Riihimaki EJ, Tahti EE. A gamma camera method for quantitation of split renal function in children followed for vesicoureteric reflux. *Pediatr Radiol* 1978; 7: 78–81.
13. Makler PT, Charkes NN, Malmud LS. Calculation of net renal uptake curves without use of a blood pool agent. *Eur J Nucl Med* 1979; 4: 339–342.
14. Diffey BL, Hall FM, Corfield JR. The ^{99m}Tc-DTPA dynamic renal scan with deconvolution analysis. *J Nucl Med* 1976; 17: 352–355.
15. Piepsz A, Dobbeleir A, Erbsmann F. Measurement of separate kidney clearance by means of ^{99m}Tc-DTPA complex and a scintillation camera. *Eur J Nucl Med* 1977; 2: 173–177.
16. Russell CD, Bischoff PG, Kontzen 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.
17. Gordon I, Colarinha P, Fettich J, Fischer S, Frokier J, Hahn K, et al. Guidelines for standard and diuretic renography in children. *Eur J Nucl Med* 2001; 28: BP21–30.
18. Fleming JS. Measurement of hippuran plasma clearance using a gamma camera. *Phys Med Biol* 1977; 22: 526–530.
19. Gates GF. Split renal function testing using Tc-99m DTPA. A rapid technique for determining differential glomerular filtration. *Clin Nucl Med* 1983; 8: 400–407.
20. Gates GF. Glomerular filtration rate: estimation from fractional renal accumulation of ^{99m}Tc-DTPA (stannous). *Am J Roentgenol* 1982; 138: 565–570.
21. Tondeur M, Piepsz A, Dobbeleir A, Ham H. Technetium 99m mercaptoacetyltriglycine gamma camera clearance calculations: methodological problems. *Eur J Nucl Med* 1991; 18: 83–86.
22. Inoue Y, Ohtake T, Yokoyama I, Yoshikawa K, Asai S, Ohtomo K. Evaluation of renal function from ^{99m}Tc-MAG3 renography without blood sampling. *J Nucl Med* 1999; 40: 793–798.
23. Kibar M, Noyan A, Anarat A. Tc-99m-*N,N*-ethylenedicysteine scintigraphy in children with various renal disorders: a comparative study with Tc-99m-MAG3. *Nucl Med Commun* 1997; 18: 44–52.
24. Ozker K, Onsel C, Kabasakal L, Sayman HB, Uslu I, Bozluolcay S, et al. Technetium-99m-*N,N*-ethylenedicysteine—a comparative study of renal scintigraphy with technetium-99m-MAG3 and iodine-131-OIH in patients with obstructive renal disease. *J Nucl Med* 1994; 35: 840–845.
25. Kibar M, Yapar Z, Noyan A, Anarat A. Technetium-99m-*N,N*-ethylenedicysteine and Tc-99m DMSA scintigraphy in the evaluation of renal parenchymal abnormalities in children. *Ann Nucl Med* 2003; 17: 219–225.
26. Gupta NK, Bomanji JB, Waddington W, Lui D, Costa DC, Verbruggen AM, et al. Technetium-99m-L,L-ethylenedicysteine scintigraphy in patients with renal disorders. *Eur J Nucl Med* 1995; 22: 617–624.
27. Piepsz A, Blaufox MD, Gordon I, Granerus G, Majd M, O'Reilly P, et al. Consensus on renal cortical scintigraphy in children with urinary tract infection. *Semin Nucl Med* 1999; 29: 160–174.
28. Wujanto R, Lawson RS, Prescott MC, Testa HJ. The importance of using anterior and posterior views in the calculation of differential renal function using ^{99}Tc^{m}-DMSA. *Br J Radiol* 1987; 60: 869–872.