

# Comparison of $^{99m}\text{Tc}$ - Ethylene Dicycysteine and $^{99m}\text{Tc}$ -Dimercaptosuccinic Acid Scintigraphy for the Evaluation of Cortical Scarring and Differential Renal Function in Children with Recurrent Urinary Tract Infection

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## ABSTRACT

**Introduction:** Urinary tract infection (UTI) is the most common and severe bacterial infection in children. Renal scarring and associated deterioration in the differential renal function is a frequent finding. Scarring may occur even in asymptomatic patients without vesicoureteric reflux.

**Materials and methods:** Fifty-three children (43 M:10 F, mean age:5.3 years; range 2-10 years) with evidence of recurrent UTI were enrolled in the study. Patients with duplex or crossed fused ectopic kidneys and with acute or chronic renal failure were excluded from the study protocol. Each patient underwent  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -EC renal scintigraphy within a period of 2 weeks.

**Results:** Analysis of results was performed by comparing the diagnostic accuracy of the summed  $^{99m}\text{Tc}$ -EC and  $^{99m}\text{Tc}$ -DMSA images for the detection of renal cortical scars and correlation (linear regression analysis) between the two renal scintigraphic procedures for the estimation of differential renal function.  $^{99m}\text{Tc}$ -DMSA imaging demonstrated scarring in 41 kidneys whereas  $^{99m}\text{Tc}$ -EC scintigraphy revealed scarring in 29/41 kidneys only. The percentage function of both kidneys with  $^{99m}\text{Tc}$ -EC and  $^{99m}\text{Tc}$ -DMSA showed good correlation. The  $r^2$  for left kidney was 0.95 and for right kidney was 0.94.

**Conclusion:**  $^{99m}\text{Tc}$ -EC scintigraphy has low sensitivity (70%) for the detection of cortical scarring as compared to  $^{99m}\text{Tc}$ -DMSA (100%) renal imaging. On the hand,  $^{99m}\text{Tc}$ -DMSA static imaging gives good estimate for the DRF and the values are in good agreement with the corresponding values derived from dynamic  $^{99m}\text{Tc}$ -EC scanning.

**Keywords:** UTI, Cortical scarring,  $^{99m}\text{Tc}$ -EC,  $^{99m}\text{Tc}$ -DMSA.

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## INTRODUCTION

The urinary tract infection (UTI) is one of the most common infections in pediatric population.<sup>1</sup> Urine is an excellent culture medium and residual urine after voiding poses a significant risk for developing an infection of the urinary

tract. Early diagnosis and treatment of UTI may prevent or decrease renal damage caused by acute febrile UTI.<sup>2</sup> Renal cortical scintigraphy with  $^{99m}\text{Tc}$ -labeled dimercaptosuccinic acid ( $^{99m}\text{Tc}$ -DMSA) is considered to be the most sensitive technique compared to ultrasonography and intravenous pyelography for detection of renal parenchymal changes in acute pyelonephritis and renal scarring.<sup>3-5</sup>

A variety of radiotracers which are in clinical use for the assessment of functional renal parameters have also been proposed for the detection of renal parenchymal disease. However, as these agents are used for performing renal dynamic imaging, therefore the patients are injected with these tracers under the camera and the dynamic study is acquired during the first few minutes before any significant pelvicalyceal accumulation of the radiotracer occurs. Thus the short acquisition time with these radiotracers still provides good temporal resolution but provides poor spatial resolution. However, renal radiotracers with a high extraction rate, such as  $^{99m}\text{Tc}$ -mercaptoacetyl-triglycine ( $^{99m}\text{Tc}$ -MAG3) and  $^{99m}\text{Tc}$ -ethylene dicycysteine ( $^{99m}\text{Tc}$ -EC) provide better quality cortical images owing to better count statistics.  $^{99m}\text{Tc}$ -EC, a metabolite of ethylene cysteine dimer, has imaging qualities similar to  $^{99m}\text{Tc}$ -MAG3.<sup>6,7</sup>

In view of the above mentioned characteristics of the renal radiotracers, the present study was carried out to compare the diagnostic utility of  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -EC in the evaluation of renal parenchymal abnormalities and differential renal function (DRF) in pediatric patients.

## MATERIALS AND METHODS

This prospective study was carried in 53 pediatric (age ranging between 2-10 years) patients who presented with the diagnosis of recurrent UTI. Children with anatomic abnormalities of upper urinary tract, such as duplex systems or crossed fused ectopic kidneys, etc. were not included in this study. Also children having acute or chronic renal failure were excluded from this study. An informed written consent was obtained from all the enrolled patients who underwent  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -EC scintigraphies within a period of 2 weeks.

Renal dynamic scintigraphy was performed immediately after the intravenous administration of 3.7 MBq/kg body weight of  $^{99m}\text{Tc}$ -EC with gamma camera head placed posterior to the patient. Prior to the study acquisition, all the patients were well-hydrated and were instructed to drink about 10 ml/kg body weight of water or other (soft drinks/milk) liquids.

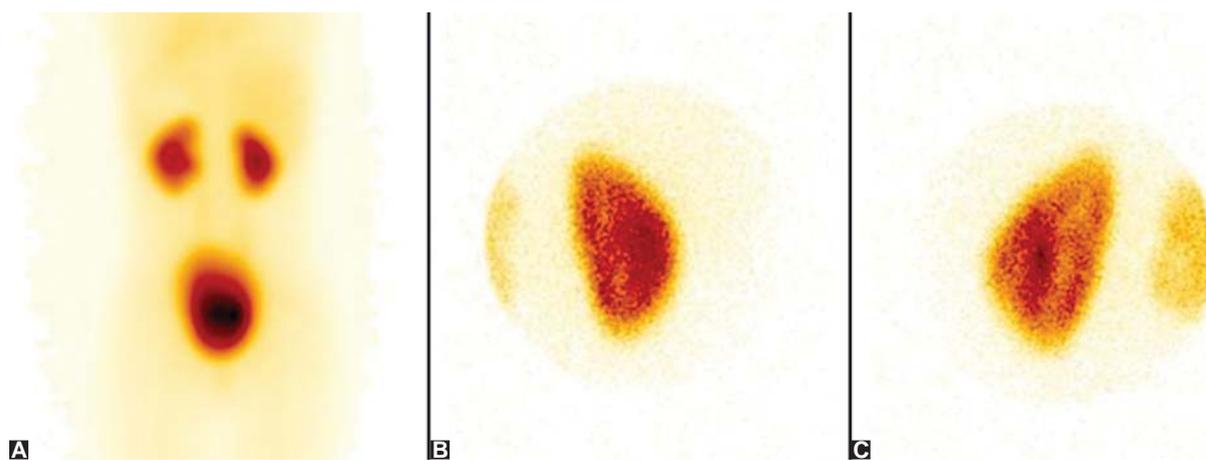
The dynamic study was acquired for 25 minutes in  $128 \times 128$  matrix (Perfusion phase: 60 frames; 1 sec/frame and Cortical phase: 48 frames: 30 sec/frame). The images were processed to obtain the DRF and were regrouped into 3 minutes image sets, and the first 3 minutes summed image was used for evaluation of renal scars. Renal cortical scintigraphy was performed 3 hours after intravenous administration of 1.5 MBq/kg body weight of  $^{99m}\text{Tc}$ -DMSA. Anterior, posterior, left posterior oblique and right posterior oblique pinhole images were acquired. DRF was calculated using background—corrected geometric mean of anterior and posterior views.

Analysis of results was performed by comparing the diagnostic accuracy of summed  $^{99m}\text{Tc}$ -EC images with

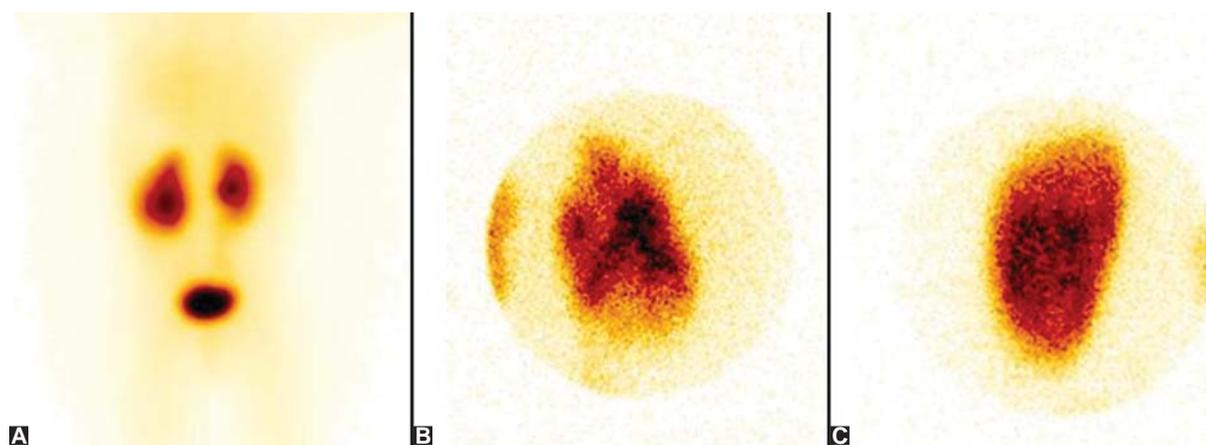
$^{99m}\text{Tc}$ -DMSA for the detection of renal cortical scars and to find out correlation, if any, between the differential renal function calculated by  $^{99m}\text{Tc}$ -EC with  $^{99m}\text{Tc}$ -DMSA. Simple linear regression analysis was performed to calculate the correlation between DRF calculated by  $^{99m}\text{Tc}$ -EC images with  $^{99m}\text{Tc}$ -DMSA.

## RESULTS

Among the 53 patients evaluated were 43 males and 10 females. The age of these patients ranged from 2 to 10 years with a mean age of 5.3 years. All the kidneys were evaluated for presence of scars by visual analysis. The images obtained from  $^{99m}\text{Tc}$ -DMSA revealed 41 scarred kidneys while 29 scarred kidneys were detected on imaging with  $^{99m}\text{Tc}$ -EC. A representative scan showing normally functioning kidneys both on  $^{99m}\text{Tc}$ -EC and  $^{99m}\text{Tc}$ -DMSA imaging is presented in Figures 1A to C. The Figures 2A to C presents normal unscarred kidneys on  $^{99m}\text{Tc}$ -EC summed images whereas the pinhole  $^{99m}\text{Tc}$ -DMSA imaging shows (Fig. 2B) scarring in the upper and lower poles of the right kidney.



**Figs 1A to C:**  $^{99m}\text{Tc}$ -EC 3-minute summed up posterior image (A),  $^{99m}\text{Tc}$ -DMSA pinhole images (B—right kidney and C—left kidney) showing uniform distribution of the radiotracer without any evidence of cortical scar (normal kidneys)



**Figs 2A to C:**  $^{99m}\text{Tc}$ -EC 3-minute summed up posterior image demonstrating no evidence of scar in any of the kidneys (A),  $^{99m}\text{Tc}$ -DMSA pinhole images indicating the presence of scar in the upper and lower poles of the right kidney (B) and normal left kidney (C)

The sensitivity and specificity of  $^{99m}\text{Tc}$ -EC summed images were 70 and 100% respectively. The percentage function of both kidneys with  $^{99m}\text{Tc}$ -EC and  $^{99m}\text{Tc}$ -DMSA showed good correlation. The  $r^2$  for left kidney was 0.95 and for right kidney was 0.94.

## DISCUSSION

$^{99m}\text{Tc}$ -DMSA scintigraphy is the most sensitive investigation for the detection of scars as well as acute pyelonephritic changes. Other modalities like pyelography ultrasound and computed tomography have been shown to have low sensitivity as compared to DMSA scintigraphy. Apart from detecting scars, accurate differential renal function also can be calculated from  $^{99m}\text{Tc}$ -DMSA images by taking the geometric mean of both anterior and posterior images.

Renal tubular radiopharmaceuticals have been used for cortical imaging due to their property of high tubular extraction. These agents also provide information regarding perfusion and differential function of kidneys, drainage of upper outflow tracts and indirect evidence of vesicoureteric reflux. Two such agents currently available are  $^{99m}\text{Tc}$ -MAG3 and  $^{99m}\text{Tc}$ -EC. The advantages of  $^{99m}\text{Tc}$ -EC include less prominent hepatic uptake and higher clearance rate as compared to that of  $^{99m}\text{Tc}$ -MAG3 mainly due to higher renal extraction ratio of the former agent. However, reports on the use of these agents for detecting focal parenchymal abnormalities have been conflicting. Some authors have reported that  $^{99m}\text{Tc}$ -MAG3 is equivalent to  $^{99m}\text{Tc}$ -DMSA for cortical imaging<sup>8,9</sup> whilst others have found it to be inferior to  $^{99m}\text{Tc}$ -DMSA.<sup>9</sup> Most authors have used a 2 to 3 minutes summed images for reporting  $^{99m}\text{Tc}$ -MAG3 scans. These summed images were found to have a sensitivity of 96% in revealing renal parenchymal defects with the specificity of only 39%.<sup>10</sup> This was because the summed  $^{99m}\text{Tc}$ -MAG3 images were noisy and give a high false-positive rate.

In the present study, we compared the diagnostic accuracy of  $^{99m}\text{Tc}$ -EC having characteristics comparable or better than  $^{99m}\text{Tc}$ -MAG3<sup>11</sup> and  $^{99m}\text{Tc}$ -DMSA for the detection of cortical scars in the study subjects. For this comparison, the first 3 minutes summed images were used to evaluate the parenchymal defects.  $^{99m}\text{Tc}$ -DMSA static (anterior and posterior) imaging revealed 41 scarred kidneys in 53 patients.  $^{99m}\text{Tc}$ -EC was able to detect only 29 defects (scars) in these kidneys. Our study showed a low sensitivity of only 70% compared to other studies.<sup>8,12,13</sup> The main difference was all these studies (except one study)<sup>13</sup> compared the planar images of two modalities while our study was done by comparing the pinhole images of  $^{99m}\text{Tc}$

-DMSA with planar images of  $^{99m}\text{Tc}$ -EC and it is a well-known fact that pinhole are superior to planar images for detecting renal scars. With such a low sensitivity for detection of scars in our study it can be assumed that sensitivity of  $^{99m}\text{Tc}$ -EC will further drop down when one has to look for early pyelonephritic changes in which cortical margins are maintained. Likewise, it has been reported earlier by Mohkam et al<sup>1</sup> that in patients with clinical signs of pyelonephritis,  $^{99m}\text{Tc}$ -DMSA renal scintigraphy can detect the disease more accurately than the other inflammatory and imaging tests.  $^{99m}\text{Tc}$ -DMSA-SPECT renal imaging offers no additional and statistical significant advantage over the planar imaging for the detection of cortical defects.<sup>14</sup> Pietrzak et al reported<sup>15</sup> that parametric clearance imaging has a higher sensitivity and accuracy for detection of regional post-inflammatory changes in the kidneys than conventional summation images ( $p < 0.05$ ) and shows parenchymal changes similar to static scintigraphy (high Cohen's kappa index). Narayana et al<sup>13</sup> compared the diagnostic accuracy of  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -EC scintigraphy for the detection of cortical scarring and observed that the overall sensitivity and specificity of  $^{99m}\text{Tc}$ -EC scanning was 93 and 96% respectively.

Other important difference in our study compared to other studies was the study population. Only one study by Narayana et al<sup>13</sup> included children with minimum one episode of UTI while other studies included patients with different renal disorders.<sup>8,12</sup> We included children with recurrent UTI giving a high pretest probability of finding scar compared to other studies where study population was heterogeneous. As studies were performed within 2 weeks of each other the possibility of resolution of scars within this period, to be missed by  $^{99m}\text{Tc}$ -EC imaging was very remote. Like other previous studies<sup>11,12</sup> the specificity of  $^{99m}\text{Tc}$ -EC in our study was 100%. This high specificity of the present study was also attributed to the observation that the patients, if any with atrophic kidneys or cystic abnormalities which can lead to false-positive findings were excluded.

## CONCLUSION

We found an excellent correlation for the estimation of differential renal function between  $^{99m}\text{Tc}$ -EC and  $^{99m}\text{Tc}$ -DMSA imaging procedures and the values of the split renal function derived by two methods can thus be used interchangeably. However, the sensitivity of  $^{99m}\text{Tc}$ -EC imaging for the detection of renal scarring was low (70%) as compared to  $^{99m}\text{Tc}$ -DMSA which is considered as gold standard investigation for the diagnosis of renal pyelonephritis/scarring.

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