

Role of radioisotope ^{99m}Tc and scintillation gamma camera in assessment of multiple renal functional indices using two different carriers DTPA & MDP

Mohammed I. A. Saif Elden¹, Waleed A. Diab², Mohamed El-Azab Farid³

¹(Physicist at department of clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt)

²(Lecturer of nuclear medicine at department of clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt)

³(Prof. Dr. at department of Physics, Faculty of Science, Assiut University, Assiut 71516, Egypt)

Abstract: Renal scintigraphy can provide the valuable split renal function which is not obtainable by other non-invasive measurements. Whole body bone scintigraphy (bone scan) using a ^{99m}Tc -labelled pharmaceutical is one of the most commonly performed radionuclide examinations. Both the osseous components of the skeletal system as well as the kidneys and bladder are visualized^[2]. This study was designed to investigate the feasibility of the assessment of relative renal function with ^{99m}Tc -MDP as compared with renal imaging radiotracers ^{99m}Tc -DTPA^[1] using a gamma camera. Clear from this study that ^{99m}Tc -MDP can give useful information for assessment of GFR instead of ^{99m}Tc -DTPA partly providing install quantity of radiopharmaceutical. As the used ^{99m}Tc -MDP for assessment of differential function (split) give the same value which can be obtained by ^{99m}Tc -DTPA nearly, regardless of quantity of radiopharmaceutical. Using ^{99m}Tc -MDP superfluous at assessment of $T_{1/2}$ and T_{peak} when compared with the value obtained by ^{99m}Tc -DTPA.

I. Introduction

^{99m}Tc -methylene diphosphonate (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 ^{99m}Tc -diethylene triamine penta acetic acid (^{99m}Tc -DTPA)^[3]. ^{99m}Tc -DTPA is a chelating agent which was introduced into renal nuclear medicine in 1970. ^{99m}Tc -DTPA is the least expensive renal radiopharmaceutical. It is cleared by the glomerulus and can be used to measure glomerular filtration rate (GFR)^[4]. The extraction fraction (the percentage of the agent extracted with each pass through the kidney) of ^{99m}Tc -DTPA is approximately 20%; for this reason, in patients with impaired renal function this radiopharmaceutical may not be as useful as those with higher extraction efficiencies such as ^{99m}Tc -mercaptoacetyltriglycine (MAG3) and iodine-131^[5].

Since ^{99m}Tc -DTPA the same ^{99m}Tc -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^[6,7].

If one can estimate renal function incidental to bone scintigraphy, it is very favorable from the view point of convenience and cost effectiveness. As one quantitative analysis of renal function, measurements of GFR are now performed in clinical practice, particularly with Gate's method^[8,9].

The purpose of the study was to compare the glomerular filtration rate (GFR) obtained by means of a modified Gates' method ^{99m}Tc -MDP with those obtained by means of ^{99m}Tc -DTPA and assessment of other renal indices.

II. Materials And Methods

Patients:

A total of 13 adult patients (1 male, 12 females) with malignant tumors were enrolled. Their ages ranged from 37 to 65 years (mean 51 ± 14), Heights ranged from 146 to 175 cm (mean 160 ± 14) and Weights ranged from 40 to 91 Kgm (mean 65 ± 25). Excluding a patient with perirenal abscess or had malignant tumors in the genitourinary tract. All the patients underwent both radionuclide studies with ^{99m}Tc -MDP and ^{99m}Tc -DTPA within period one week.

Renography with ^{99m}Tc -DTPA:

^{99m}Tc -DTPA was prepared according to the manufacturer's instructions with the kits in radioisotope laboratory in Nuclear Medicine Department of Oncology and Nuclear Medicine, Assiut University Hospitals, Egypt. Using a commercially available kits. Counts in pre-injection and post-injection syringes were measured for 60 seconds at 30 cm from the Gamma-Camera (MARCONI AXIS2, VT TECHNOLOGY INC, CLEVELAND, OHIO 44143, USA), to determine the net amounts of activity injected. Each patient was hydrated with 200 ml of water 30 minutes before the examination. Renography was carried out with the patient in a supine position with the gamma-camera detector placed under the patient's bed. Rapid injection of 5 mCi of ^{99m}Tc -DTPA was given through an end welling butterfly needle in an antecubital vein and was followed by infusion of 10 ml of normal saline. Immediately after tracer arrival within the kidneys, data acquisition was performed for 31 minutes (1 sec per frame for 60 sec and 15 sec per frame for 1800 sec) with a scintillation camera 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 x 64 matrix on a computer processing system (MARCONI MEDICAL SYSTEMS, ODYSSEY FX 810, COMPAQ), serial interval dynamic 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 aquastions. On completion of renography with 5 mCi of ^{99m}Tc -MDP, the remaining 15 mCi 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 pelvicalyceal dilation as well as whole body skeleton by two experienced nuclear physicians.

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 GFR of each kidney, Split (Differential GFR), T_{peak} (time from injection to time of maximum count rate), and $T_{1/2}$ (The half emptying time) were obtained.

Estimation of Total and Split GFR:

The GFR was determined by a modified Gates' method¹⁸. 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.

III. Results

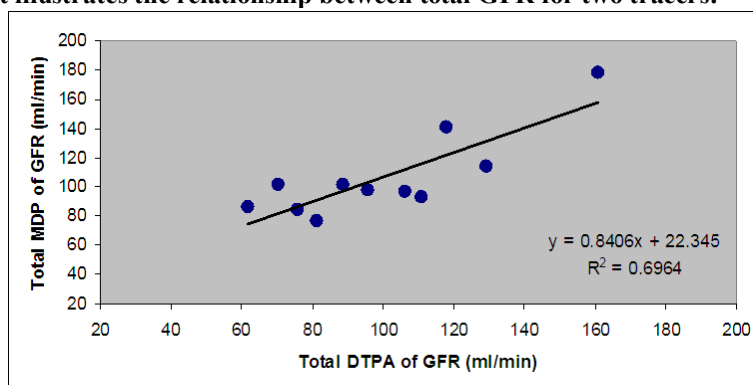
The GFR obtained by means of ^{99m}Tc -MDP were compared with those obtained by means of ^{99m}Tc -DTPA, and the feasibility of the assessment of renal function with ^{99m}Tc -MDP was investigated.

GFR Patterns:

Fifty-two value of GFR were obtained on (13) patients using ^{99m}Tc - DTPA and ^{99m}Tc -MDP tracers. Of (12) paired Equal in the same value, (10) paired convergent in the value and (4) paired different in the value.

Total GFR:

The following chart illustrates the relationship between total GFR for two tracers:

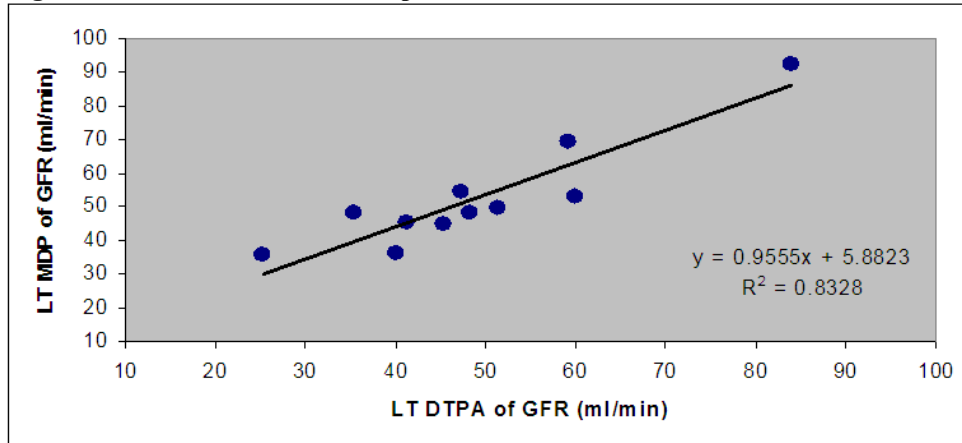


(Figure 1)

(Figure 1) shows correlation between total GFR (ml/min) obtained by means of the two tracers. We excluded points (1 & 2) from the chart because the patient's number (1 & 2) showed big difference in GFR values because there is differences in dose of radiopharmaceutical used ^{99m}Tc -MDP (20 mCi) VS ^{99m}Tc -DTPA (5 mCi).

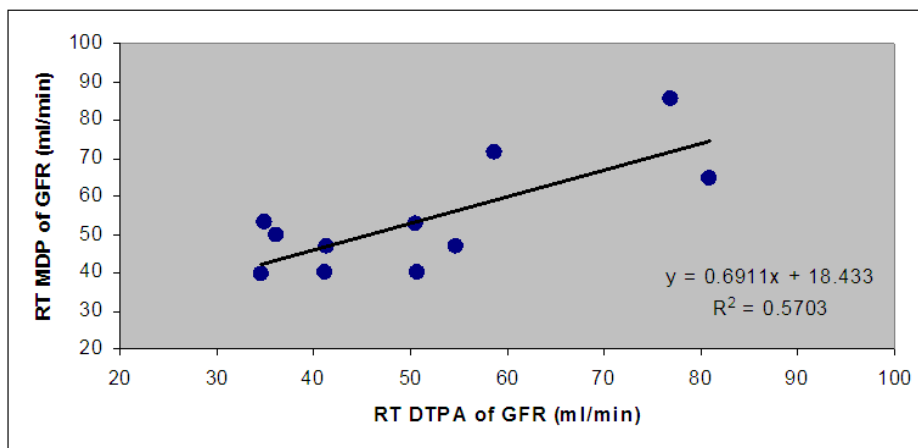
Left and Right kidney:

The following chart illustrates the relationship between two tracers:



(Figure 2)

(Figure 2) shows correlation between left GFR (ml/min) obtained by means of the two tracers.

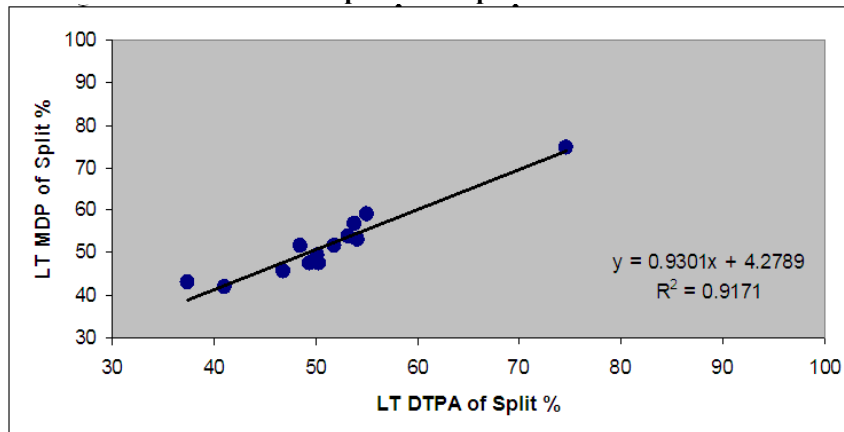


(Figure 3)

(Figure 3) shows correlation between right GFR (ml/min) obtained by means of the two tracers. We excluded points (1 & 2) from the chart for the reasons mentioned above.

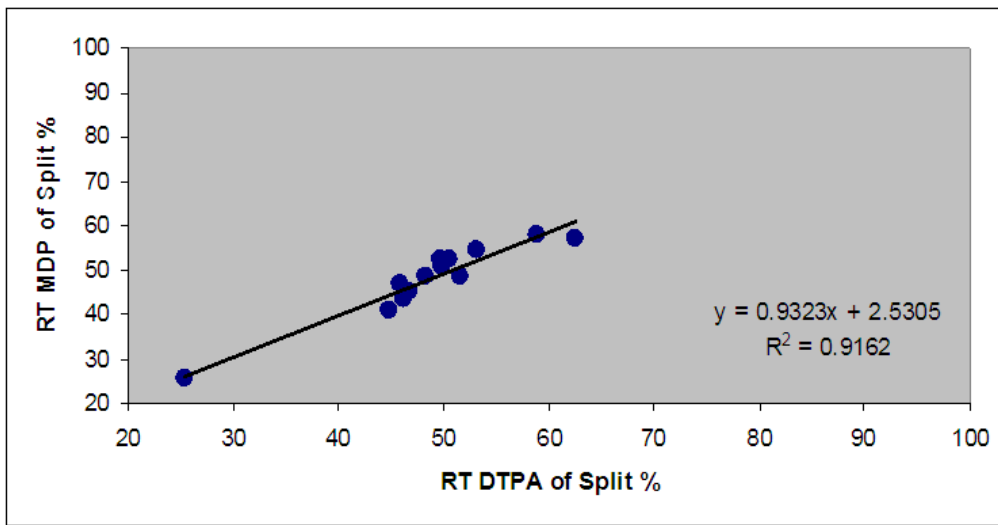
Split Patterns:

The following chart illustrates the relationship between split for two tracers:



(Figure 4)

(Figure 4) correlation between differential GFR (ml/min) of left kidney obtained by means of the two tracers.

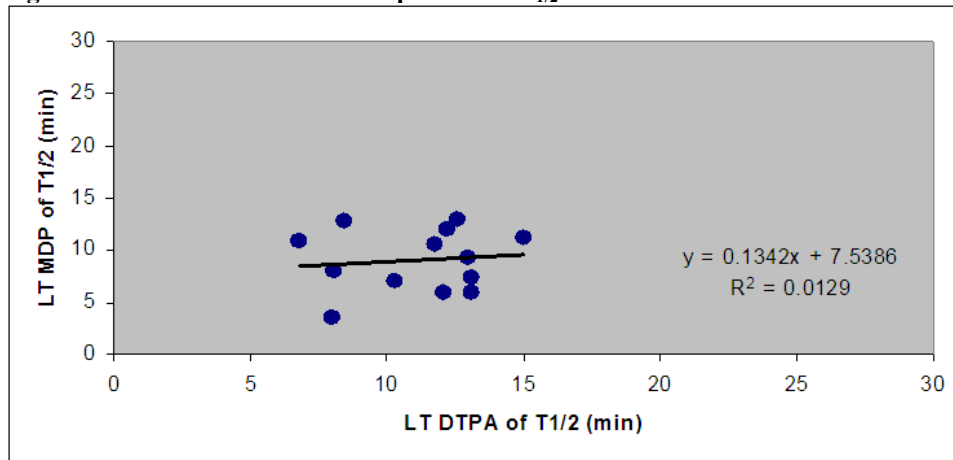


(Figure 5)

(Figure 5) correlation between differential GFR (ml/min) of left kidney obtained by means of the two tracers.

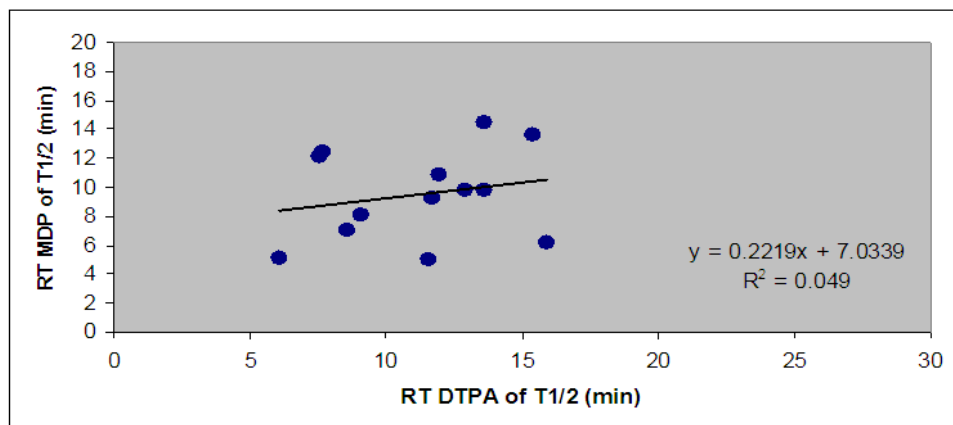
$T_{1/2}$ Patterns:

The following chart illustrates the relationship between $T_{1/2}$ for two tracers:



(Figure 6)

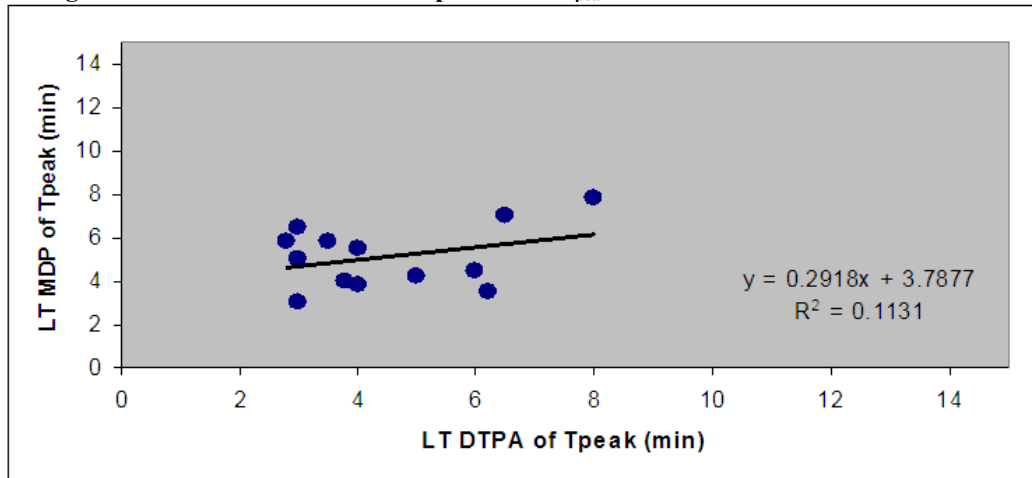
(Figure 6) correlation between $T_{1/2}$ GFR (ml/min) of left kidney obtained by means of the two tracers.



(Figure 7)

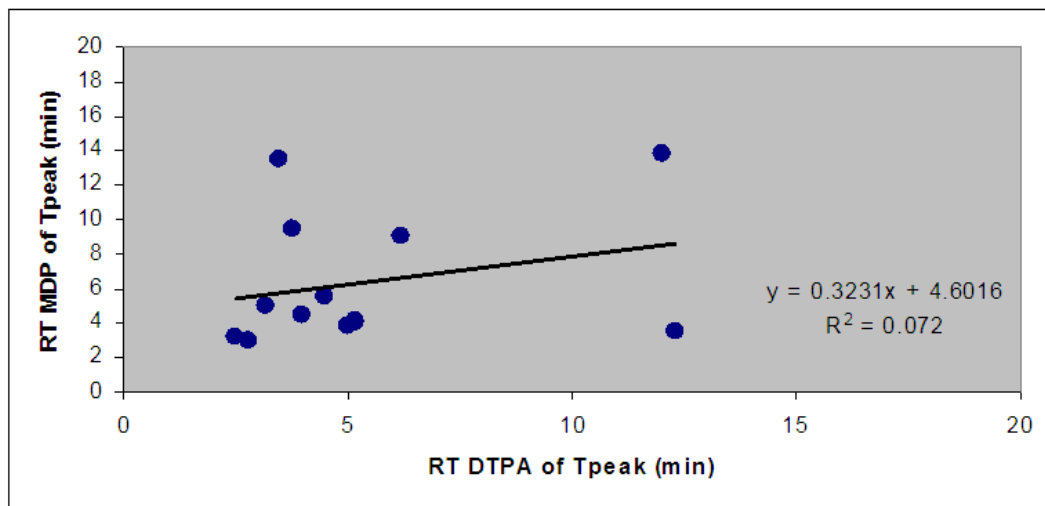
(Figure 7) correlation between $T_{1/2}$ GFR (ml/min) of right kidney obtained by means of the two tracers.
 T_{peak} Patterns:

The following chart illustrates the relationship between T_{peak} for two tracers:



(Figure 8)

(Figure 8) correlation between T_{peak} GFR (ml/min) of left kidney obtained by means of the two tracers.



(Figure 9)

(Figure 9) correlation between T_{peak} GFR (ml/min) of right kidney obtained by means of the two tracers.

IV. Discussion

Many authors have reported a number of renal abnormalities discovered incidentally on bone scintigraphy^[10]. 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^[11].

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.

Therefore, we compared the GFR 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. The correlation between GFR obtained by ^{99m}Tc -DTPA and those obtained by ^{99m}Tc -MDP in (ml/min/1.73m²). Many methods have been proposed to estimate the GFR with ^{99m}Tc -DTPA^[3,12]. Of these methods, Gate's method using the gamma camera is the most common which showed that the 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^[13,14].

Renographies with ^{99m}Tc-MDP similar information concerning flow and function to those provided by renographies for ^{99m}Tc-DTPA, but the application of ^{99m}Tc-MDP to renography gives rise to significant problems because this tracer accumulates in the skeleton. However a variety of patients with increased renal uptake of ^{99m}Tc-pyrophosphate have been observed in studies of urinary tract obstruction, post chemotherapy^[15], metastatic calcification^[16], renal vein thrombosis^[17], radiation nephritis^[18], iron overload^[19], acute tubular necrosis, administration of heparin^[20], and nephrotoxic drugs^[21], it is certain that the bio distribution of ^{99m}Tc-MDP can be affected these various conditions. In order to obtain GFR, the percent uptake of 2 to 3 minutes after the radionuclide appearance in the kidneys was used. This gives information regarding renal morphology and renal function incidental to bone scintigraphy with ^{99m}Tc-MDP^[22]. If further information is of interest, more definitive renal studies should be performed with ^{99m}Tc-DTPA^[23].

Estimation of GFR

Total GFR:

Review the chart for total kidney note that there is a difference between two tracers ^{99m}Tc-DTPA and ^{99m}Tc-MDP this was the difference in the first phase, the phase of the experiment where the quantity of radiopharmaceutical differed between two tracers (1 & 2). But installs quantity of radiopharmaceutical for two tracers note Total GFR was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.83$, $p<0.002$) respectively. It is known that if the value of (r) correlation coefficient from $0.7 \rightarrow <1$ is indicate a strong positive linear relationship^[24] so we have obtained value is located in this range. The value we have obtained is different from that obtained from (Khalil and et al.,2013) ($r=0.96$, $p<0.001$) because the study course different ,they chose patients with diagnosed with hydronephrosis or underwent a therapeutic operation. But our patients selected on the basis that they do not suffer from the disease in the kidneys so that's maybe the back of this difference.

Left kidney

Review the chart for left kidney after the exclusion of points (1 & 2) note left GFR was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.91$, $p<0.001$) respectively. The value we have obtained is indicate a strong positive linear relationship^[24] and teeny different from that obtained from (Khalil and et al.,2013) for the reason mentioned above.

Right kidney

Review the chart for right kidney after the exclusion of points (1 & 2) we find right GFR was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.76$, $p<0.008$) respectively. The value we have obtained is indicate a strong positive linear relationship^[24] and teeny different from that obtained from (Khalil and et al.,2013) for the reason mentioned above.

Estimation of split

Left split

Review the chart for left kidney without excluding any points we find left Split was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.96$, $p<0.001$) respectively. This result is indicate a strong positive linear relationship^[24] and largely consistent with that obtained by (Khalil and et al.,2013)

Right split

Review the chart for right kidney without excluding any points we find right Split was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.96$, $p<0.001$) respectively. This result is indicate a strong positive linear relationship^[24] and largely consistent with that obtained by (Khalil and et al.,2013)

Estimation of T_{1/2}

Left T_{1/2}

From chart without excluding any points we find left T_{1/2} was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.11$, $p<0.8$) respectively. It is indicate a weak positive linear relationship^[24].

Right T_{1/2}

From chart without excluding any points we find left T_{1/2} was obtained by means of ^{99m}Tc-MDP correlated well with those obtained by means of ^{99m}Tc-DTPA ($r=0.22$, $p<0.5$) respectively. It is indicate a weak positive linear relationship^[24]. This variable (T_{1/2}) has not been fully discussed by (Khalil and et al.,2013)

Estimation of T_{peak}

Left T_{peak}

From chart without excluding any points we find left T_{peak} was obtained by means of ^{99m}Tc -MDP correlated well with those obtained by means of ^{99m}Tc -DTPA ($r=0.34$, $p<0.3$) respectively. It is indicate a moderate positive linear relationship^[24].

Right T_{peak}

From chart without excluding any points we find right T_{peak} was obtained by means of ^{99m}Tc -MDP correlated well with those obtained by means of ^{99m}Tc -DTPA ($r=0.27$, $p<0.4$) respectively. It is indicate a moderate positive linear relationship^[24]. This variable (T_{peak}) has not been fully discussed by (Khalil and et al.,2013)

V. Conclusion

The assessment of renal function with ^{99m}Tc -MDP can be performed incidental to bone scintigraphy and is expected to provide useful information in monitoring renal function.

The early characteristics of renal handling of ^{99m}Tc -MDP are sufficiently similar to those of ^{99m}Tc -DTPA with the installation of the quantity of radiopharmaceuticals for two tracers. So that, accurate estimation of differential (split) renal function are possible with this agent, and that ^{99m}Tc -MDP determined renal differential most likely reflects differential glomular filtration rate even with a difference of the quantity of radiopharmaceuticals for tow tracers, and both kidneys were normal or abnormal. With reference to $T_{1/2}$ and T_{peak} the results show, which was obtained significant difference between tow tracers.

References

- [1]. (Buckley, Orla a; O'Keefe, Sylvia a; Geoghegan, Tony a; Lyburn, Ian D. b; Munk, Peter L. c; Worsley, Dan c; Torreggiani, William C. a, Nuclear Medicine Communications. 28(7):521-527, July 2007).
- [2]. (Khalil et al, Comparative Study Between ^{99m}Tc -MDP and ^{99m}Tc -DTPA as a Predictor For Renal Function ,Australian Journal of Basic & Applied Sciences;Feb2013, Vol. 7 Issue 2, p360,2013)
- [3]. (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).
- [4]. (Goates et al.,1990.Comparison of methods for calculating glomerular filtration rate: technetium- ^{99m}Tc -DTPA scinti-graphic analysis, protein-free and whole-plasma clearance of technetium- ^{99m}Tc -DTPA and iodine-125-iothalamate clearance. Nucl. Med., 31:424-429.
- [5]. (Taylor, A. and J.V. Nally, 1995. Clinical applications of renal scintigraphy. Am. J. Roentgenol. (AJR), 164(1): 31-41.).
- [6]. (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.).
- [7]. (Haden HT, Katz PG, Konerding KF. Detection of obstructive uropathy by bone scintigraphy. J Nucl Med 1988; 29: 1781-1785.)
- [8]. 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.
- [9]. Itoh, K., S. Tsushima, E. Tsukamoto, N. Tamaki, 2003. Reappraisal of single-sample and gamma camera methods for determination of the glomerular filtration rate with ^{99m}Tc -DTPA. Ann Nucl Med., 14: 143-150.
- [10]. (<http://www.jsnm.org/files/paper/anm/ams153/ANM15-3-09.txt>)
- [11]. (Bilchik TR, Spencer RP. Bladder variants noted on bone and renal imaging. Clin Nucl Med 1993; 18: 60-67.)
- [12]. (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.)
- [13]. Awdeh, M., K. Kouris, I.M. Hassan and H.M. Abdel Dayem, 1990. Factors affecting the Gates' measurement of glomerular filtration rate. Am J Physiol Imaging, 5(1): 36-41.
- [14]. Taylor, A., 1999. Radionucleidrenography: a personal approach. Semin. Nucl. Med., 102-127.
- [15]. Lutrin, C., C. Cameron, M. Richard, Z. Michael, J. Susan, A. Ezra, 1994. Panic disorder and chest pain: A study of cardiac stress scintigraphy patients. Am J of Kidney Dis., 74: 296-298.
- [16]. Aktas, A. and M. Haberal, 2005. Classification of ^{99m}Tc -DTPA renograms based on the relationship between uptake and perfusion pattern. Transplant Proc., 37(10): 4259-65.
- [17]. Lamki, L.M. and J.K. Wyatt, 1983. Renal Vein Thrombosis as a Cause of Excess Renal Accumulation of Bone Seeking Agents. Clin. Nucl. Med., 8: 267.
- [18]. Saha, G.B., 2010. Fundamental of nuclear Pharmacy, 6th ed. Instruments for Radiation Detection and Measurement, pp: 277-278.
- [19]. Choy, D., P.C. Murray and R. Hoschel, 1981. The effect of iron on the biodistribution of bone scanning agents in humans. Radiology, 140: 197.
- [20]. Challa, S. and J.F. Miller, 1998. Extraskelatal Uptake of Technetium- ^{99m}Tc -MDP in Sites of Heparin Administration. J. Nucl. Med., 39: 893.
- [21]. Bernard, M.S., M. Hayward, C. Hayward and L. Mundy, 1990. Evaluation of intense renal parenchymal activity ("hot kidneys") on bone scintigraphy. Clin. Nucl. Med., 15(4): 254-6.
- [22]. Bostom, A.G., F. Kronenberg, E. Ritz, 2002. Predictive performance of renal function equations for patients with chronic kidney disease and normal serum creatinine levels. J. Am. Soc. Nephrol., 13: 2140-2144.
- [23]. Taylor, A. and D. Eshima, 1994. Renal artery stenosis and ischemia: effect of renal blood flow and extraction fraction. Hypertension, 23(1): 96-103.
- [24]. <http://www.dmstat1.com/res/TheCorrelationCoefficientDefined.html>