

## Evaluating the Efficacy of Bone Tracer $^{99m}\text{Tc}$ -MDP in Detecting Individual Renal Function Compared to Renal Cortical Imaging Agent $^{99m}\text{Tc}$ -DMSA

Magda S. Hanafy<sup>1\*</sup>, Maged Abdelgalil Hamed<sup>2</sup> and Heba M. Elshafai<sup>3</sup>

<sup>1</sup>Department of Biophysics, Faculty of Science, Zagazig University, Egypt

<sup>2</sup>Department of Radiology, Faculty of Medicine, Zagazig University, Egypt

<sup>3</sup>Faculty of Science, Zagazig University, Egypt

\*Corresponding author: Magda sayed Hanafy, Professor, Department of Biophysics, Faculty of Science, Zagazig University, Zagazig, Sharkeya 44519, Egypt, Tel: +201000141384; E-mail: [omnia.hilal@yahoo.com](mailto:omnia.hilal@yahoo.com)

Received date: Jun 15, 2015, Accepted date: Aug 21, 2015, Publication date: Aug 24, 2015

Copyright: © 2015 Hanafy MS, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License; which permits unrestricted use; distribution; and reproduction in any medium; provided the original author and source are credited.

### Abstract

This study was performed to evaluate the usefulness of bone tracer  $^{99m}\text{Tc}$ -MDP in detecting renal disorders by imaging of renal cortex for patients with cortical defect and estimation of split renal function (SRF) as compared with renal cortical imaging agent  $^{99m}\text{Tc}$ -DMSA. In this study 23 patients (6 males, 17 females) with range age of 16y -75y (mean  $45.6y \pm 17.4y$ ), and a total of 46 studies (using both  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -MDP per patient for left and right kidneys) were performed for detecting renal disorders. Both studies were performed within 48 hours between each other. SRF was calculated in all cases from renal uptake of the tracers into the region of interest by using computer acquired data of gamma camera. For detecting renal cortex abnormalities, all cortical scars and defects scars seen on  $^{99m}\text{Tc}$ -DMSA scan were also detected by  $^{99m}\text{Tc}$ -MDP.

The results showed that the non visualized kidney on  $^{99m}\text{Tc}$ -DMSA scan was also non visualized on  $^{99m}\text{Tc}$ -MDP. Also, there was a high correlation between SRF values obtained from  $^{99m}\text{Tc}$ -MDP and  $^{99m}\text{Tc}$ -DMSA, where ( $p > 0.01$ ,  $r = 0.93$  for left kidney and  $r = 0.92$  for right kidney).

The similar SRF values of  $^{99m}\text{Tc}$ -MDP and  $^{99m}\text{Tc}$ -DMSA allow to use of  $^{99m}\text{Tc}$ -MDP tracers for detecting both of bone and renal abnormalities.

**Keywords:**  $^{99m}\text{Tc}$ -MDP;  $^{99m}\text{Tc}$ -DMSA; Renal cortex; Split renal function

### Introduction

Estimation of split renal function is a particularly important role of renal scintigraphy [1] and one of the major contributions of radionuclide renal studies to the practice of urology [2]. Functional and morphologic investigations with radionuclide studies play a prominent role in the diagnosis and follow-up of various renal disorders [3-7].  $^{99m}\text{Tc}$ -DMSA is slowly cleared from the blood and concentrates in the renal cortex; 42 % of the injected dose remains in the renal cortex at 6 hours [8]. DMSA is an excellent agent for detecting focal abnormalities of the renal cortex. Because of its high kidney uptake, it has been suggested that  $^{99m}\text{Tc}$ -DMSA may be the best technetium agent for determining the relative functional renal mass. Technetium-99m dimercaptosuccinic acid ( $^{99m}\text{Tc}$ -DMSA) was introduced in 1974 and is still the agent of choice for static renal scintigraphy [9,10], and  $^{99m}\text{Tc}$  MDP (methylene diphosphate) labeled phosphate complexes were first introduced in 1971 as a major advance in skeletal image. Bone scintigraphy, so far, is still a useful examination for the clinical diagnosis, especially in evaluating and following up the status of cancer patients with suspicious bony metastasis. Many authors [10-14] found that there are a number of renal disorders detected while doing bone scintigraphy because  $^{99m}\text{Tc}$ -MDP (is excreted through the kidneys to provide adequate visualization of the urinary tract. Furthermore, damage to the kidney is caused by

chemotherapy and/ or radiation therapy when the kidneys are included in the radiation field [15]. Kirkinen [16] and other investigators [17] indicated that further that urethral obstruction from radiation therapy might occur as early as three weeks or as late several years after therapy, it was potentially curable. Therefore, the estimation of renal function as well as the detection of bone metastases is useful in patients that received radiation therapy for detecting undermine renal disorders, and prevent those with high risk of renal abnormalities from going to irreversible stage.

### Material and Methods

#### Subject

A total of 46 studies for 23 patients (within ages ranged from 16 years-75years old) were performed between 2014 and 2015, in Nuclear Medicine division-Radiology department at Zagazig University Hospital, (Egypt). Because of various renal disorders and for routine indications, such as evaluation of renal cortex after urinary tract infection, the split renal function assessment (SRFs) were calculated using both  $^{99m}\text{Tc}$ -MDP and  $^{99m}\text{Tc}$ -DMSA renal scintigraphy. All studies were performed using both radionuclides for each patient to evaluate the usefulness of bone seeking radiopharmaceutical in detecting renal abnormalities as compared with renal cortical agent. All radionuclide studies were carried out using a Dual-headed gamma camera equipped with a low-energy, high-resolution parallel-hole collimator (GE Healthcare Unveils Discovery NM 630 SPECT).

During imaging, the collimator was set as close as possible to the patient's table.

### <sup>99m</sup>Tc-DMSA scintigraphy

There is no preparation for patients during a DMSA Scan, they can eat and drink normally. The radiopharmaceutical was prepared according to the manufacturer's instruction with the kit. Patients were injected with activity 5.0 mci of the radiopharmaceutical followed by infusion of 20 ml of normal saline. After 2-3 hours intravenous injection, <sup>99m</sup>Tc-DMSA static images were acquired in 256 x 256 matrix with the patients in a supine position that appears the best position to minimize renal depth difference, thus improving the accuracy of split renal function measurement and with gamma camera's detectors placed in a posterior and anterior views (250 kcounts/view or 5 minutes/view). SRFs were calculated, semi-automatically, by the geometrical mean of the anterior and posterior images, using GE Xeleris software.

### <sup>99m</sup>Tc-MDP scintigraphy

<sup>99m</sup>Tc-MDP Static images were performed on another day, for comparison with <sup>99m</sup>Tc-DMSA Static images for the same patients. Data collection and analysis were repeated under the same conditions, and SRFs for all patients were calculated by the same method.

### Data Analysis

Using the posterior and anterior digital images, regions of interest are placed around both kidneys and below both kidneys for background subtraction. Then, the background corrected counts in each kidney and the percent of total counts (DMSA uptake) in each kidney are calculated. Cross-correlation coefficients were calculated by Pearson correlation for comparison of repeated measurements of SRF for both kidneys using both radiopharmaceuticals. Statistical analysis was performed using the SPSS 14.0 software program.

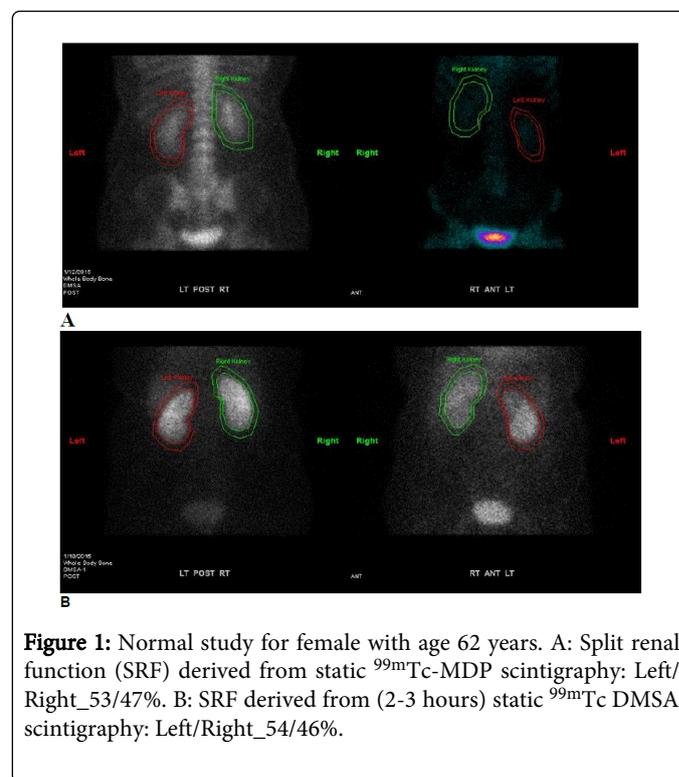
### Results

SRFs measured by <sup>99m</sup>Tc-MDP and <sup>99m</sup>Tc-DMSA renal scintigraphy are shown in Table 1. In this study, there are 9 patients had normal SRF (45%-55%) as shown in Figure 1, and 14 patients had abnormal SRF, and non visualized kidneys on <sup>99m</sup>Tc-DMSA scan were also non visualized on <sup>99m</sup>Tc-MDP. For detecting renal cortex abnormalities, all cortical scars and defects scars seen on <sup>99m</sup>Tc-DMSA scan were also detected by <sup>99m</sup>Tc-MDP as shown in Figures 2-4. In correlation analysis, there was a high correlation between the SRF obtained from the <sup>99m</sup>Tc-DMSA and <sup>99m</sup>Tc-MDP for both left and right kidneys ( $p > 0.01$  and  $r = 0.93$ ,  $r = 0.92$  left and right kidney, respectively) as shown in Figures 5 and 6.

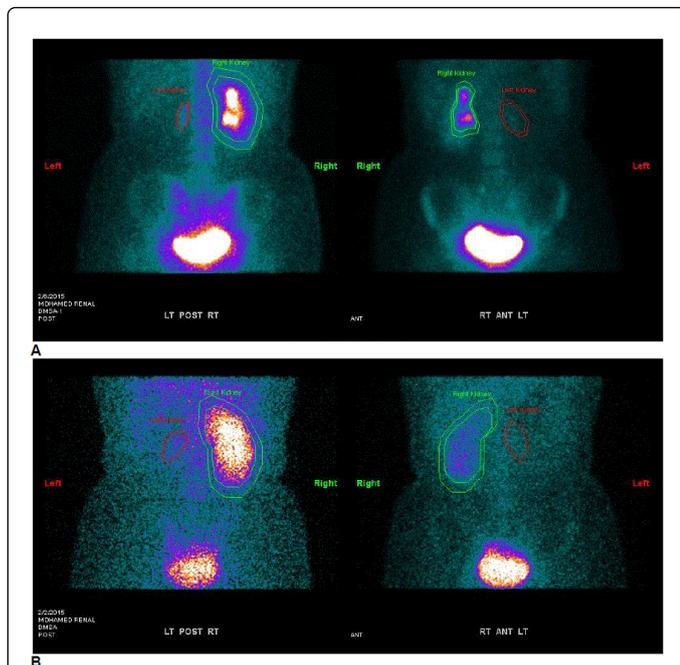
No. of case	Age	Sex	SRF by MDP		SRF by DMSA	
			LT	RT	LT	RT
1	16	F	12	88	10	90
2	19	M	6	94	13	87
3	21	F	32	68	78	22
4	22	F	1	99	2	98
5	24	F	45	55	46	54

6	29	M	38	63	48	52
7	34	F	8	92	8	92
8	37	F	55	45	54	46
9	45	F	55	45	56	44
10	46	F	42	58	47	53
11	48	F	53	47	52	48
12	49	F	49	51	48	52
13	50	M	92	8	92	8
14	51	F	50	50	52	48
15	52	F	18	82	15	85
16	54	F	0	100	0	100
17	55	F	53	47	54	46
18	57	F	59	41	60	40
19	62	F	53	47	54	46
20	64	F	89	11	88	12
21	68	M	21	79	21	79
22	70	M	42	56	39	61
23	75	M	46	54	48	52

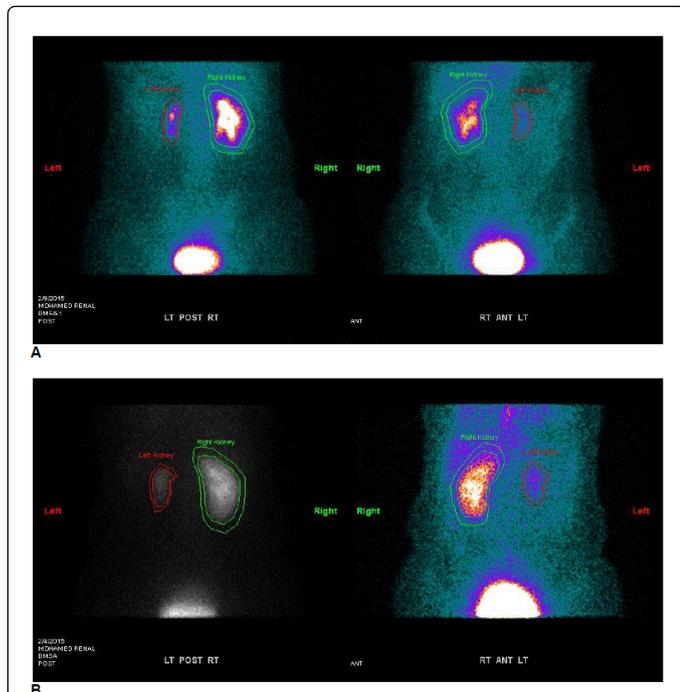
**Table 1:** SRFs measured by <sup>99m</sup>Tc-MDP and <sup>99m</sup>Tc-DMSA renal scintigraphy.



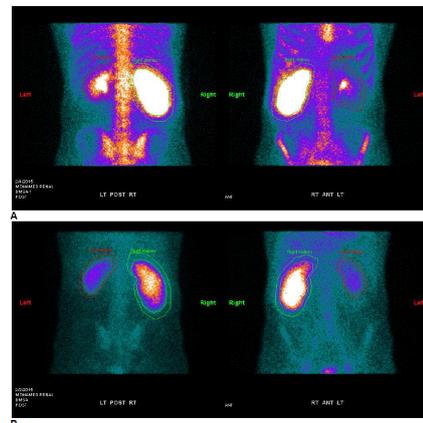
**Figure 1:** Normal study for female with age 62 years. A: Split renal function (SRF) derived from static <sup>99m</sup>Tc-MDP scintigraphy: Left/Right\_53/47%. B: SRF derived from (2-3 hours) static <sup>99m</sup>Tc DMSA scintigraphy: Left/Right\_54/46%.



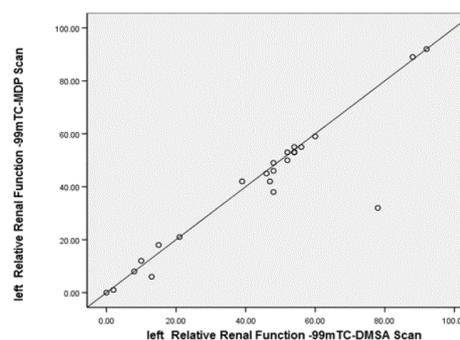
**Figure 2:** Abnormal study for female with age 22 years with left cortical defects seen on both studies. A: SRF derived from static  $^{99m}\text{Tc}$ -MDP scintigraphy: Left/Right\_2/98%. B: SRF derived from (2-3 hours) static  $^{99m}\text{Tc}$ -DMSA scintigraphy: Left/Right\_1/9%.



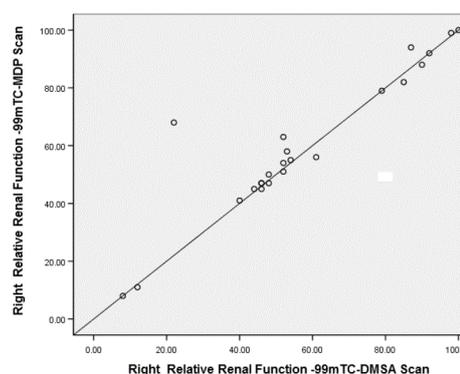
**Figure 3:** Abnormal study for female with age 34 years with left cortical defects seen on both studies. A: SRF derived from static  $^{99m}\text{Tc}$ -MDP scintigraphy: Left/Right\_8/92%. B: SRF derived from (2-3 hours) static  $^{99m}\text{Tc}$ -DMSA scintigraphy: Left/Right\_8/92%.



**Figure 4:** Abnormal study for male with age 19 years with left cortical defects seen on both studies. A: SRF derived from static  $^{99m}\text{Tc}$ -MDP scintigraphy: Left/Right\_6/94%. B: SRF derived from (2-3 hours) static  $^{99m}\text{Tc}$ -DMSA scintigraphy: Left/Right\_13/87%.



**Figure 5:** Correlation between left Split Renal Function (SRF) using  $^{99m}\text{Tc}$ -MDP versus  $^{99m}\text{Tc}$ -DMSA.



**Figure 6:** Correlation between Right Split Renal Function (SRF) using  $^{99m}\text{Tc}$ -MDP versus  $^{99m}\text{Tc}$ -DMSA.

## Discussion

$^{99m}\text{Tc}$ -DMSA scanning has been regarded as the best method for assessing SRF because the radiotracer is retained [18], primarily in the proximal convoluted tubules, for a sufficiently long time to allow static imaging of tubular activity which can be performed over several minutes [19]. It is well known that information about renal abnormalities can be obtained from bone scintigraphy because  $^{99m}\text{Tc}$ -MDP is excreted through the kidneys to provide adequate visualization of the urinary tract [20]. 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 [10-14]. In addition, detailed views of bladder can be obtained. Based on the data of animal and human studies,  $^{99m}\text{Tc}$ -MDP, unlike chelates (e.g.  $^{99m}\text{Tc}$ -DTPA) which are handled by glomerular filtration [20,21], is probably excreted as simple phosphates by renal tubular [22]. Thus, accompany with sufficient excretory amount of MDP, it provides excellent images on kidney at the time of bone scanning. So  $^{99m}\text{Tc}$ -MDP and  $^{99m}\text{Tc}$ -DMSA examinations should be performed on different days.

Technetium-99m DMSA scintigraphy is the gold standard for evaluation of Split renal function (SRF) [23-25].  $^{99m}\text{Tc}$ -dimercaptosuccinic acid ( $^{99m}\text{Tc}$ -DMSA) is an agent that is actively taken up by the proximal and distal renal tubular cells, directly from per tubular vessels, not secreted to the tubular lumen [26] and accumulates in the renal cortex [27]. This modality is primarily used for imaging functioning cortical mass and individual renal function [28] since the abnormal kidney function was set at <45% for one kidney [29]. It is the most reliable method for assessing chronic cortical scarring [19]. In the  $^{99m}\text{Tc}$ -DMSA studies, SRF is calculated using the geometric mean and taking kidney depth into account by acquiring images, anteriorly and posteriorly.  $^{99m}\text{Tc}$ -MDP is currently recognized as the most common radiopharmaceutical tool in detecting skeletal metastasis. After injection, the agent shows a biexponential type of blood clearance. The exponent I represents bone uptake and the exponent II, mainly is the renal excretion. It is generally agreed that the cumulative renal excretion up to 3 hours ranged between 30-50% [21,23,30]. So, by high resolution gamma cameras, we can visualize excellent renal image and dynamic derangement of urinary excretion at the time of bone scanning [20]. Park [20] and Vieras [31] showed that the detection rate for renal abnormality was 97.4%. Wen-sheng state that  $^{99m}\text{Tc}$ -MDP used in detecting renal abnormalities may improve the selection of patients for excretory urography, and prevent those with high risk of renal abnormalities from going to irreversible stage. In another study compared with  $^{99m}\text{Tc}$ -MDP and  $^{99m}\text{Tc}$ -DTPA scintigraphy for assessment renal function, the author state that the feasibility of the assessment of renal function with  $^{99m}\text{Tc}$ -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. Miyazaki [27] found that SRF derived from the  $^{99m}\text{Tc}$ -DTPA scintigraphy showed a good correlation with results obtained from the  $^{99m}\text{Tc}$ -DMSA scan. They found the mean SRF value of the  $^{99m}\text{Tc}$ -DTPA scintigraphy to be 2% different than that of the  $^{99m}\text{Tc}$ -DMSA. In this study there was a high correlation between the SRF obtained from the  $^{99m}\text{Tc}$ -DMSA and  $^{99m}\text{Tc}$ -MDP or both left and right kidneys.

## Conclusion

The result confirmed that  $^{99m}\text{Tc}$ -MDP scintigraphy can simultaneously estimate split renal function and skeletal lesions, it is valuable for saving time, effort and money because the patients have  $^{99m}\text{Tc}$ -MDP scintigraphy did not need another renal examination if the individual renal function is the clinical question but assessment of global renal function as well as GFR cannot evaluated with these modalities and further evaluation with more specific renal imaging agents is recommended.

## Compliance with Ethical Standards

**Funding:** This study was funded by the authors.

## Conflict of Interest

There is no any conflict interest among the authors.

## Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Informed Consent

Informed consent was obtained from all individual participants included in this study.

## References

1. Shokeir AA, Gad HM, el-Diasty T (2003) Role of radioisotope renal scans in the choice of nephrectomy side in live kidney donors. *J Urol* 170: 373-376.
2. Piepsz A, Blaufox MD, Gordon I, Granerus G, Majd M, et al. (1999) Consensus on renal cortical scintigraphy in children with urinary tract infection. Scientific Committee of Radionuclides in Nephrourology. *Semin Nucl Med* 29: 160-174.
3. Gordon I, Anderson PJ, Lythgoe MF, Orton M (1992) Can technetium-99m-mercaptoacetyltriglycine replace technetium-99m-dimercaptosuccinic acid in the exclusion of a focal renal defect? *J Nucl Med* 33: 2090-2093.
4. Hackstein N, Buch T, Rau WS, Weimer R, Klett R (2007) Split renal function measured by triphasic helical CT. *Eur J Radiol* 61: 303-309.
5. Daniel GB, Mitchell SK, Mawby D, Sackman JE, Schmidt D (1999) Renal nuclear medicine: a review. *Vet Radiol Ultrasound* 40: 572-587.
6. Yura T, Takamitsu Y, Yuasa S, Miki S, Takahashi N, et al. (1991) Total and split renal function assessed by ultrasound Doppler techniques. *Nephron* 58: 37-41.
7. Kowalsky RJ, Perry JR (1987) Radiopharmaceutical in Nuclear Medicine. Appleton and Lang: 329-333.
8. Constable AR (1982) Bone scintigraphy in nephrourology. Academic press, London, Toronto, Sydney: 313-319.
9. Maisey M (1908) Imaging the skeleton with radionuclides. In: Nuclear Medicine-A clinical introduction. Update books, London Dordrecht, Boston: 42-45.
10. Adams KJ, Shuler SE, Witherspoon LR, Neely HR (1980) A retrospective analysis of renal abnormalities detected on bone scans. *Clin Nucl Med* 5: 1-7.
11. Chayes ZW, Strashun AM (1980) Improved renal screening on bone scans. *Clin Nucl Med* 5: 94-97.

12. Koizumi K, Tonami N, Hisada K (1981) Diffusely increased Tc-99m-MDP uptake in both kidneys. Clin Nucl Med 6: 362-365.
13. Jacobson AF (1995) Diffuse renal retention on bone scintigraphy in localized clear-cell renal epithelial neoplasm. J Nucl Med 36: 817-819.
14. Muram D, Oxorn H, Curry RH, Drouin P, Walters JH (1981) Postradiation ureteral obstruction: a reappraisal. Am J Obstet Gynecol 139: 289-293.
15. Kirkinen P, Kauppila A, Kontturi M (1980) Treatment of ureteral strictures after therapy for carcinoma of the uterus. Surg Gynecol Obstet 151: 487-490.
16. Richie JP, Withers G, Ehrlich RM (1979) Ureteral obstruction secondary to metastatic tumors. Surg Gynecol Obstet 148: 355-357.
17. Rossleigh MA (2001) Renal cortical scintigraphy and diuresis renography in infants and children. J Nucl Med 42: 91-95.
18. Summerlin AL, Lockhart ME, Strang AM, Kolettis PN, Fineberg NS, et al. (2008) Determination of split renal function by 3D reconstruction of CT angiograms: a comparison with gamma camera renography. AJR Am J Roentgenol 191: 1552-1558.
19. Park CH, Glassman LM, Thompson NL, Mata JS (1973) Reliability of renal imaging obtained incidentally in <sup>99m</sup>Tc-polyphosphate bone scanning. J Nucl Med 14: 534-536.
20. Weber DA, Keyes JW, Wilson GA, Landman S (1976) Kinetics and imaging characteristics of <sup>99m</sup>Tc-labeled complexes used for bone imaging. Radiology 120: 615-621.
21. Subramanian G, McAfee JG, Bell EG, Blair RJ, O'Mara RE, et al. (1972) <sup>99m</sup>Tc-labeled polyphosphate as a skeletal imaging agent. Radiology 102: 701-704.
22. Castronovo FP Jr, Callahan RJ (1972) New bone scanning agent: <sup>99m</sup>Tc-labeled 1-hydroxy-ethylidene-, 1-disodium phosphonate. J Nucl Med 13: 823-827.
23. Ardelia Diaz E, Miguel Martinez B, Gutierrez Duenas JM, Diez Pascual R, Garcia Arcal D, et al. (2002) Comparative study of differential renal function by DMSA and MAG-3 in congenital unilateral uropathies. Cir Pediatr 15: 118-121.
24. Piepsz A (2002) Cortical scintigraphy and urinary tract infection in children. Nephrol Dial Transplant 17: 560-562.
25. Lythgoe MF, Gradwell MJ, Evans K, Gordon I (1998) Estimation and relevance of depth correction in paediatric renal studies. Eur J Nucl Med 25: 115-119.
26. Lythgoe MF, Gradwell MJ, Evans K, Gordon I (1998) Estimation and relevance of depth correction in paediatric renal studies. Eur J Nucl Med 25: 115-119.
27. Miyazaki C, Harada H, Shuke N, Okizaki A, Miura M, et al. (2010) (<sup>99m</sup>Tc)-DTPA dynamic SPECT and CT volumetry for measuring split renal function in live kidney donors. Ann Nucl Med 24: 189-195.
28. Ritchie G, Wilkinson AG, Prescott RJ (2008) Comparison of differential renal function using technetium-99m mercaptoacetyltriglycine (MAG3) and technetium-99m dimercaptosuccinic acid (DMSA) renography in a paediatric population. Pediatr Radiol 38: 857-862.
29. Smellie J, Edwards D, Hunter N, Normand IC, Prescod N (1975) Vesico-ureteric reflux and renal scarring. Kidney Int Suppl 4: S65-72.
30. Krishnamurthy GT, Tubis M, Endow JS, Singhi V, Walsh CF, et al. (1974) Clinical comparison of the kinetics of <sup>99m</sup>Tc-labeled polyphosphate and diphosphonate. J Nucl Med 15: 848-855.
31. Vieras F, Boyd CM (1975) Diagnostic value of renal imaging incidental to bone scintigraphy with <sup>99m</sup>Tc-phosphate compounds. J Nucl Med 16: 1109-1114.

This article was originally published in a special issue, entitled: "**Medical radiation techniques**", Edited by Aruna Turaka, Fox Chase Cancer Center, USA