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MEASUREMENT OF UPTAKE BY USING IMAGE BASED BIO-DISTRIBUTION OF ^{99m}Tc-DTPA AND ^{99m}Tc-DMSA FOR KIDNEY, LIVER AND SPLEEN

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ABSTRACT

Measurement of uptake by using the image based bio-distribution of ^{99m}Tc-DMSA (Dimercapto succinic acid) and ^{99m}Tc-DTPA (Diethylene triaminepenta acetic acid) in Kidney, Spleen and Liver with frame to frame analysis has been evidenced as the simplified way than the existing computer program based methodology, like MIRD and others. In this study, 100 patients were included in each scan. For ^{99m}Tc-DTPA scan, the mean uptake percentage for Kidney was 84.06% and that for Spleen was 7.80% and for Liver was 8.13% in which 66 patients were male and 34 were female age ranging from 3 (three) months to 70 (seventy) years. On the other hand,^{99m}Tc-DMSA scan was executed for 60 (sixty) male and 40 (forty) female patients; the mean values of uptake percentage for Kidney, Spleen and Liver were 87.40%, 5.99% and6.60% respectively. It was manifested that the uptake percentages of radiopharmaceuticals were the highest in kidney for youngers whereas those values in other organs were lower than adults.

Key words: Image based bio-distribution, ^{99m}Tc-DTPA, ^{99m}Tc-DMSA

INTRODUCTION

Renal scan is a diagnostic procedure that uses nuclear medicine to examine the anatomy and functioning of kidneys. In a nuclear medicine, renal scan, images are obtained by the delivery of fluid into the kidneys via blood stream, concentration of wastes in the kidney and excretion or flow from kidneys through the ureters and filling of the bladder. During this procedure, a radioactive material, called a radioisotope or radionuclide “tracer”, is injected into vein of a patient. The radioisotope releases gamma rays which can be detected by gamma camera or scanner from the outside of the body. Several related experiments have been performed with different radiopharmaceuticals technetium-99mdimercaptosuccinic acid (^{99m}Tc-DMSA), technetium-99m diethylenetria-minepenta acetic acid (^{99m}Tc-DTPA) as well as technetium-99m mercaptoacetyltriglycine (^{99m}Tc-MAG3) and in the modern eratechnetium-99 m ethylene dicysteine (^{99m}Tc-EC) scans with some variable conditions, among them, age, type of kidney diseases associated

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with uptake efficiency are noteworthy. Renal scintigraphy has been used to determine the relative renal shape and function for long duration. Renal uptake of ^{99m}Tc-DMSA as a function of time and correlation between ^{99m}Tc-DMSA and ^{99m}Tc-DTPA in renal uptake were experienced (Itoh *et al.*1990). Notwithstanding, various types of radiopharmaceuticals such as ^{99m}Tc-DMSA, ^{99m}Tc-DTPA, ^{99m}Tc-MAG3 as well as latterly ^{99m}Tc-EC have been used worldwide in renal scintigraphy (Moran 1999). All of these can be prepared accurately to analyze the relative renal function, although there is enormous variation in properties among these radiopharmaceuticals (Taylor and Lallone 1985). Therefore, ^{99m}Tc-DMSA as a significant tracer of static renal scan is considered the most reliable procedure to evaluate relative renal function and the most befitting tracer for renal cortical imaging (Ardela *et al.*2002, Kawashima *et al.*1998, Piepsz 2002, Piepsz *et al.*1999, Bingham and Maisey 1978). The binding level to protein in mammals of ^{99m}Tc-DMSA is approximately 90%, this binding characteristic forecloses momentous glomerular filtration and ^{99m}Tc-DMSA principally admits into the kidney through peritubular extraction (Verbruggen *et al.*1992). It is initially applied in human for cortical imaging and reckoning of functional renal mass (Daniel *et al.*1999, Muller and Gutsche 1995, Campbell and Powers 2003). Detection of pyelonephritis and renal scars can be comprehended by applying in human (Majd and Rushton 1992, Hitzel *et al.*2004, Shanon *et al.*1992). For evaluating glomerular filtration rate (GFR) evaluation in mammals, ^{99m}Tc-DTPA is exercised for as much as no tubular secretion or reabsorption is observed but it is thoroughly filtered by the glomerulus (Daniel *et al.*1999, Campbell and Powers 2003, Majd and Rushton 1992, Hitzel *et al.*2004, Shanon *et al.*1992, Urhan *et al.*2007). In a few experiments, it has been emphasized that relative renal function calculated with ^{99m}Tc-DTPA is as reliable as ^{99m}Tc-DMSA (Lee *et al.*2010). From another point of view, a couple of studies, it has observed that ^{99m}Tc-DTPA is not as effective as 99mTc-DMSA in calculating relative renal structure (Domingues *et al.*2006). As there is ambiguity in the reliability of ^{99m}Tc-DTPA for the calculation of relative renal function and there is limited study related to relative renal function calculation according to the variation of age; we retrospectively designed a study to compare the relative uptake of ^{99m}Tc-DMSA and ^{99m}Tc-DTPA based on image formed by scintillation camera. Because, from the deeds mentioned above, it can be noted that image based bio-distribution in DMSA scan and DTPA scan such as uptake percentage (count) in different organ (Heart, Spleen, Liver etc.) were not experienced yet. For this reason, it is one of the easiest ways to determine the uptake percentage in targeted organ and other organ which indicates the purity of radio-pharmaceuticals as well.

METHODS AND MATERIALS

Basically, bio-distribution of any radiopharmaceutical is measured by calculating cumulated activity of each organ and attenuation factor for existing computer based

program like MIRD. But the aim of this image based bio-distribution study was to make easier the procedure of measuring uptake (absorbed dose) in each organ such as, kidney, spleen, liver etc. by drawing ROI (region of interest) curve as shown in figure 1 to obtain the counts and standard deviation. Attenuation factor may be neglected because of remaining approximately analogous.

For Medical Internal Radiation Dosimetry (MIRD) (Snyder 1975), the dose imparted to a target volume k from a single source volume h, can be calculated as:

$$D(r_k \leftarrow r_h) = \tilde{A}h_S(r_k \leftarrow r_h) \quad \text{(i)}$$

Where,

$\tilde{A}_h$ = cumulated activity in the source organ

S = average dose absorbed by the target organ per unit of cumulated activity in source organ.

The cumulated activity in *h* is defined as the total number of disintegrations in that organ, i.e. the integral of the activity A over the time:

$$\tilde{A}_h = \int_0^\infty \tilde{A}_h(t)dt \quad \text{(ii)}$$

The S factor can be defined as:

$$D(r_k \leftarrow r_h) = \sum_i \Delta_i \Phi_i (r_k \leftarrow r_h)/m_k \quad \text{(iii)}$$

Where,

Δ_i = the average energy emitted per transision as i-th radiation

Φ_i = the absorbed fraction i.e. the fraction of the energy emitted in the source volume r_h which was absorbed in the target volume r_k and

m_k = the mass of target.

In general, if several organs accumulate the radiopharmaceutical, the overall dose to the target volume (organ or tissue) *k* is obtained by summing up all the contribuions coming from the various coming from the various regions *h*:

$$D(rk) = \sum_h \tilde{A}h \sum_i \Delta_i \Phi_i (r_k \leftarrow r_h)/m_k \quad \text{(iv)}$$

This experiment was carried out at National Institute of Nuclear Medicine and Allied Sciences (NINMAS, BSMMU Campus).Generally, for dynamic scan, after pre syringe count dynamic sequential sixty images of the kidneys obtained in the posterior position immediately after i/v administration of ^{99m}Tc-DTPA (RENON, Code: MR11, manufacturer: MEDI-RADIOPHARMA LTD.) and the study would be continued for thirty minutes whereas Diuretic was given after 12 or 13 minutes and for static scan, six images obtained in multiple projections three hours post injection after i/v administration

of ^{99m}Tc-DMSA (MERCAPTON, Code: MR13, manufacturer: MEDI-RADIOPHARMA LTD.) were taken to calculate uptake and standard deviation with the help of medical software named Siemens SYNGO 2009A package.

In this study, posterior viewed image for static scan and the image got immediately at $T_{1/2}$ period (in which uptake remains higher than other frames) for dynamic scan was selected to draw region of interest (ROI) shown in figs. 1 and 2 respectively and calculate

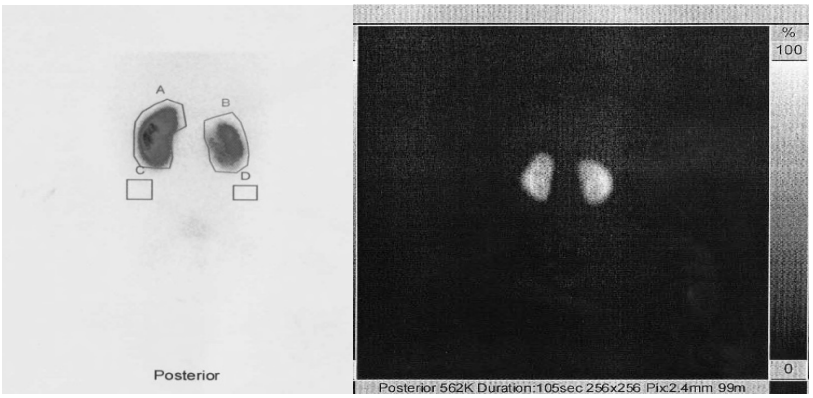

Fig. 1. ROI drawing inscanned image of ^{99m}Tc-DMSAin posterior view (left)and normal raw image (right).

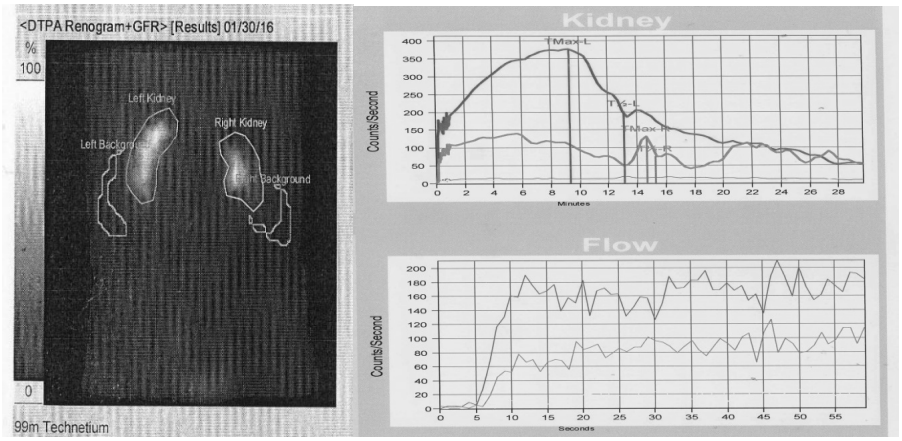

Fig. 2. ROI drawing inscanned image of ^{99m}Tc-DTPAin posterior view (left) and count/sec. vs time graph for kidney(right).

absorbed dose by Kidney, Liver and Spleen. Rational image might be so helpful that the disorder of an organ be detected easily as the gamma rays emitted from radiopharmaceuticals, administrated to a patient, and were detected using a standard two headed gamma camera (Anger 1964). Methods excluding Gamma camera may not capable to construct an image of an optical object such as human organs or body.

For ^{99m}Tc-DTPA scan, 100 patients were analyzed in which 66 patients were male and 34 were female with ages ranging 3 (three) months to 70 (seventy) years having different features such as, age, chronical as well as non-chronical diseases and other distinguishable qualities in our experiment. In addition, for ^{99m}Tc-DMSA scan, another 100 patients consisted of 60 (sixty) patients were male and 40 (forty) patients were female within the age range 2 (two) months to 62 (sixty-two) years were also analyzed. The doses were 3±1 mCi for children and 6±1 mCi for adult patients. Avoiding complexities, average uptake value of different organ of all patients had been taken.

RESULTS

The percentage of radiopharmaceuticals purity was always above 95% belonging to the accepted range for both ^{99m}Tc-DTPA and ^{99m}Tc-DMSA. But most of the days of experiment, this percentage was 97%. So, any major deviation in image quality was not experienced.

For ^{99m}Tc-DTPA scan, the mean uptake percentage of 100 patients in which 66 patients were male and 34 were female with ages ranging 3 (three) months to 70 (seventy) years of Kidney was 84.06%, Spleen was 7.80% and Liver was 8.13%. For the age range 0 to 20 years, the mean uptake percentage of Kidney was 85.82%, Spleen was 6.76% and Liver was 7.40%, for 20 to 40 years, the mean uptake percentage of Kidney was 84.56%, Spleen was 7.71% and Liver was 7.71% and for 40 years above the mean uptake of Kidney was 79.95%, Spleen was 9.92% and Liver was 10.11%. The results are presented in Table 1 and illustrated in Figs. 3 and 4.

Table 1. Reference absorbed dose provided by tracer kit manufacturer (left) and Average counts for ^{99m}Tc-DTPA Scan (right)

^{99m}Tc-RENON	Absorbed dose per unit activity administered by intravenously (mGy/MBq)				
ORGAN	Adult	15 years	10 years	5 years	1 year
Adrenals	1.4E-03	1.8E-03	2.7E-03	4.2E-03	7.8E-03
Bladder walls	6.5E-02	8.1E-02	1.2E-01	1.7E-01	3.2E-01
Bone surfaces	1.7E-03	2.1E-03	3.1E-03	4.6E-03	8.5E-03
Breast	9.4E-04	9.4E-04	1.4E-03	2.2E-03	4.3E-03
Stomach wall	1.3E-03	1.7E-03	2.8E-03	4.1E-03	7.5E-03
Small intestine	2.6E-03	3.1E-03	5.0E-03	7.5E-03	1.3E-02
ULI wall	2.2E-03	2.9E-03	4.4E-03	7.1E-03	1.2E-02
LLI wall	4.2E-03	5.4E-03	8.2E-03	1.1E-02	1.9E-02
Kidneys	4.4E-03	5.4E-03	7.7E-03	1.1E-02	2.0E-02
Liver	1.3E-03	1.6E-03	2.5E-03	3.9E-03	7.0E-03
Lungs	1.0E-03	1.3E-03	2.0E-03	3.1E-03	5.7E-03
Ovaries	4.3E-03	5.3E-03	7.8E-03	1.1E-02	1.8E-02
Pancreas	1.5E-03	1.8E-03	2.9E-03	4.5E-03	8.1E-03
Red Marrow	2.5E-03	3.0E-03	4.2E-03	5.7E-03	8.7E-03
Spleen	1.4E-03	1.7E-03	2.5E-03	4.0E-03	7.2E-03
Testes	2.8E-03	4.1E-03	6.8E-03	1.0E-02	1.9E-02
Thyroid	7.9E-04	1.3E-03	2.1E-03	3.4E-03	6.1E-03
Uterus	7.9E-03	9.6E-03	1.5E-02	2.1E-02	3.5E-02
Other tissue	1.7E-03	2.0E-03	3.1E-03	4.6E-03	8.3E-03
Effective dose equivalent (mSv/MBq)	6.3E-03	7.8E-03	1.1E-02	1.7E-02	3.0E-02

Age	Kidney%	Spleen%	Liver%
0 to 20 years	85.8272	6.7657	7.4071
20 to 40 years	84.5669	7.7160	7.7171
Above 40	79.9538	9.9273	10.1189
Average	84.0604	7.8064	8.1331

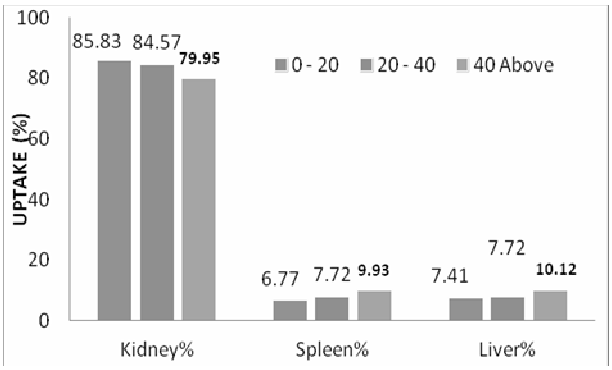

Fig. 3: Classified histogram of uptake percentage for dynamic scan according to age.

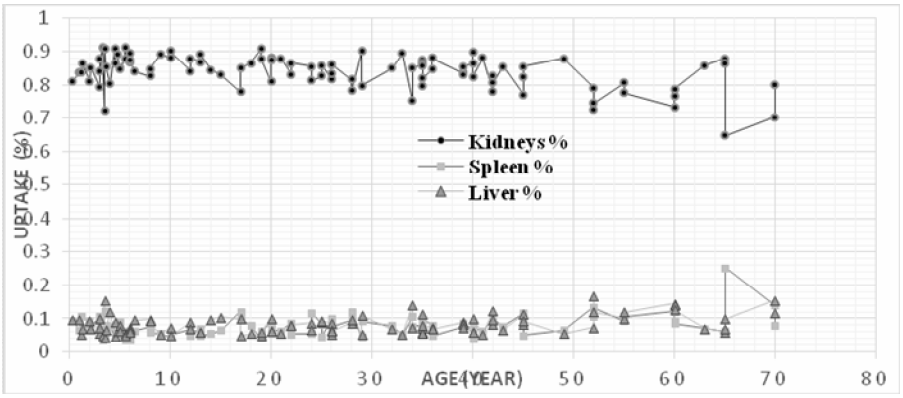

Fig. 4. variation of uptake percentage according to age for DTPA scan.

For ^{99m}Tc-DMSA scan, 100 patients consisted of 60 (sixty) patients were male and 40 (forty) patients were female within the age range from 2 (two) months to 62 (sixty-two) years the mean uptake percentage of Kidney was 87.40%, Spleen was 5.99% and Liver was 6.60%. When we classified the patients according to their age, it was noticed that the uptake percentage of radiopharmaceutical in kidney for youngsters was higher than others. For the age range of 0 to 20 years, the mean uptake percentage of Kidney was 87.58%, Spleen was 5.87% and Liver was 6.54%, for 20 to 40 years, the mean uptake percentage of Kidney was 86.67%, Spleen was 6.28% and Liver was 7.03% and for 40 years above the mean uptake percentage of kidney was 84.30%, Spleen was 6.98% and Liver was 8.71% shown in Table 2 (right) and depicted in Figs. 5 and 6.

Table 2: Reference absorbed dose provided by tracer kit manufacturer (left) and Average counts for ^{99m}Tc-DMSA Scan (right).

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 year	10 year	5 year	1 year
Adrenals	1.3E-02	1.6E-02	2.4E-02	3.5E-02	6.0E-02
Bladder wall	1.9E-02	2.4E-02	3.5E-02	5.1E-02	9.4E-02
Bone surfaces	3.5E-03	4.3E-03	6.4E-03	9.9E-03	1.9E-02
Breast	1.8E-03	1.8E-03	2.8E-03	4.5E-03	8.4E-03
Stomach wall	5.5E-03	6.3E-03	9.8E-03	1.3E-02	2.0E-02
Small intestine	5.2E-03	6.4E-03	1.0E-02	1.5E-02	2.5E-02
ULI wall	5.1E-03	6.3E-03	9.6E-03	1.4E-02	2.3E-02
LLI wall	3.2E-03	4.2E-03	6.7E-03	1.0E-02	1.8E-02
Kidneys	1.7E-01	2.1E-01	2.9E-01	4.2E-01	7.3E-01
Liver	9.7E-03	1.2E-02	1.8E-02	2.5E-02	4.1E-02
Lungs	2.5E-03	3.5E-03	5.2E-03	8.0E-03	1.4E-02
Ovaries	3.7E-03	4.6E-03	7.2E-03	1.1E-02	2.0E-02
Pancreas	9.0E-03	1.1E-02	1.6E-02	2.3E-02	3.7E-02
Red marrow	6.3E-03	7.5E-03	1.0E-02	1.4E-02	2.0E-02
Spleen	1.3E-02	1.7E-02	2.6E-02	3.8E-02	6.1E-02
Testes	1.8E-03	2.4E-03	3.9E-03	6.2E-03	1.2E-02
Thyroid	1.1E-03	1.9E-03	3.1E-03	5.1E-03	9.2E-03
Uterus	4.6E-03	5.5E-03	8.9E-03	1.3E-02	2.3E-02
Other tissue	3.0E-03	3.6E-03	5.2E-03	8.0E-03	1.4E-02
Effective dose equivalent (mSv/MBq)	**1.6E-02**	**1.9E-02**	**2.7E-02**	**4.0E-02**	**6.9E-02**

Age	Kidney%	Spleen%	Liver%
0 to 20 years	87.5849	5.8744	6.5407
20 to 40years	86.6741	6.2879	7.0380
Above 40	84.3039	6.9857	8.7104
Average	87.4025	5.9947	6.6028

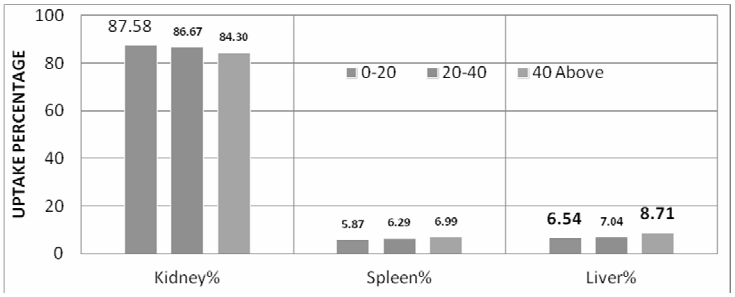

Fig. 5. Classified histogram of uptake percentage for static scan according to age.

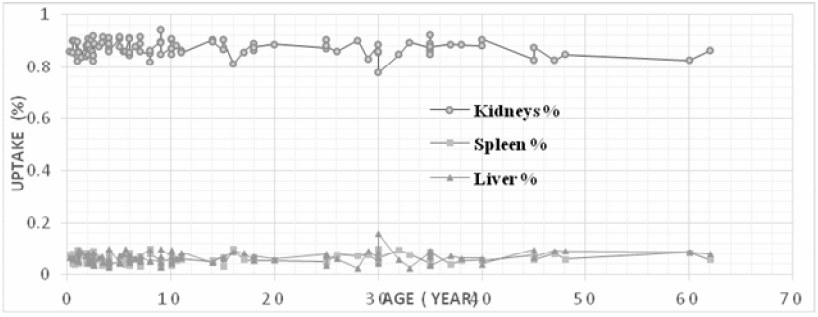

Fig. 6. Variation of uptake percentage according to age for DMSA scan.

DISCUSSION

The measurement taken in our study was not amazeballs way than the computer program based methodology to determine the uptake percentage for targeted organ and other organs because cumulated activity, attenuation factor was unheeded in our study due

to avoid complexities in calculation. As attenuation factor was the kindred for the ratio of uptake counts of two organs. For this reason, average values were taken into consideration to establish this procedure more uncomplicated. This study demonstrated that the uptake percentage of kidney for the age range of 2 (two) months to 20 (twenty) years was higher than that of adult people. Mostly, the relative proportion of uptake in spleen and liver was lower for 2 (two) months to 20 (twenty) years and medium for 20 (twenty) to 40 (forty) years and higher for the patients of above 40 years. The quality of scanned images was almost analogous because of having tagging efficiency within accepted reference value (higher than 95%).The uptake percentage varied for different aged people due to enormous reasons. A number of drugs which can alter kidney function interfere with kidney imaging. In patients with unilateral renal artery stenosis, angiotensin converting enzyme inhibitors such as captopril decrease glomerular filtration in the affected kidney by interruption of auto regulatory mechanisms (Nally and Black 1992). This is increasingly used in interventional studies to improve the diagnosis of renal vascular disease. Dipyridamole, at concentrations used in cardiac stress testing, has been shown to affect kidney handling of ^{99m}Tc- DTPA in human volunteers for up to 15 min after completion of dipyridamole infusion (Latham *et al.*1992). Another notable reasons are distinct anatomical and physiological properties, variation of food habit, different types of diseases (such as, Percutaneous Nephrolithotripsy on Renal Function, proximal tubular dysfunction), characteristics adopted from heredity (Moskovitz *et al.* 2006, Verber and Meller 1989, Smellie *et al.* 1988, Van Luyk *et al.* 1983, Ben-Haim *et al.* 2000).

CONCLUSION

Evaluation of bio-distribution taken only posterior viewed image for static scan using ^{99m}Tc-DMSA and image formed at the $T_{1/2}$ period for dynamic scan using ^{99m}Tc-DTPA with frame to frame analysis has been manifested as more convenient way than existing methods to evaluate internal doses of organs. Imaged based bio-distribution can be deviated through ROI marking and background counts of the radiopharmaceuticals of targeted organ (In our study Kidney) but the results are well correlated with the reference values of the tracer pharmaceuticals.

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