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Assessment of Relative Kidney Function in KOREA NUCLEAR Medicine Study Evaluation of the Effectiveness of Geometric Mean According to Kidney Depth

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Abstract

When measuring relative renal function ratio(RRFR) in nuclear medicine tests, radiation is usually counted using a posterior detector. However, when there is a difference in the depth of the left and right kidneys, counting of the radiation using only the posterior detector may result in a lower counting rate of the deeply located kidneys.

In this study, we investigated the usefulness of geometric mean in measuring the RRFR by applying a geometric mean after counting radiation using the anterior-posterior detector when the depths of the left and right kidneys are different.

Kidney model studies and clinical studies were performed using the Symbia T16 gamma camera system to obtain anterior and posterior images. For RRFR calculations, RRFR was measured by applying arithmetic mean, once with information only counted by the posterior detector. Again, with the information counted by the anterior and posterior detectors, the geometric mean was applied to measure the RRFR.

The results of the kidney model study were y = 0.23 + 0.38x, R2 = 0.986(p = 0.000), and the clinical results were y = 0.25 + 0.16x and R2 = 0.823(p = 0.000). It can be seen that as the depth difference of the elongation increases, the function ratio of the deeply located elongation increases gradually among the RRFRs in which the geometric mean is applied with the information counted by the anterior and posterior detectors.

In kidney examinations conducted by the nuclear medicine department, the RRFR is generally measured using only the posterior detector. However, when the RRFR was measured using the geometric mean with the information from the anterior and posterior detectors, it was confirmed that the function ratio of the deeply located kidney rises. The above results suggest that the attenuation between the kidney and the detector is corrected. For patients with different depths of the left and right kidneys, it would be useful to measure the RRFR by applying a geometric mean with the both detectors.

[Keywords] ***Nuclear Medicine Safety, Kidney Model, MAG3 Renal Scan, Geometric Mean, Relative Renal Function***

1. Introduction

The kidney is a bean-shaped organ, weighing about 150 mg and it exists bilaterally in the back of the lower abdomen. Typically, as the right kidney is located inferior to the liver, so the left kidney is slightly more superior than it. The kidney is an organ that maintains a uniform in vivo environment and excretes waste product. It also, has endocrine functions, which maintain homeostasis and produce and activate hormones[1].

Evaluations of kidney size, shape, function and disease include urinalysis, pyelography, sonography, computed tomography(CT), magnetic resonance imaging(MRI), and nuclear medicine scan; nuclear medicine scans are utilized for the diagnosis of renal disease, decisions regarding therapeutic intervention, and follow-up[2].

99mTc-DTPA(99mtechnetiumdiethylene-mine pentaacetic Acid), or I-131 OIH(Iodine-131 orthoiodohippurate) in bolus[3][4][5].

99mTc-MAG3 is currently the most widely used radiopharmaceutical for the dynamic renal scan in many hospitals instead of 99mTc-DTPA and hippuran. It is a type of triamidemercaptide(N_3S) complex, with an excretion rate of 0.6-0.7, which is three times that of 99mTc -DTPA. It shows higher binding to plasma protein than hippuran(90%), has smaller distribution volume, and shows about 5% erythrocyte consumption. Kidney/background site ratio is 3.7 on average, which is about twice that of 99mTc-DTPA[6].

Dynamic renal scan using 99mTc-MAG3 dynamically provides continuous visualization of the process of radiopharmaceutical uptake into the kidney and its excretion. After 99mTc-MAG3 is injected-intravenously, the scan dynamically visualizes the kidney and urinary tract. The acquired image is used to evaluate renal function after quantitative analysis[7].

99mTc-MAG3 dynamic renal scan comprises of three phases. The first phase is the vascular, filling phase in which radioactivity rapidly increases in the kidney during the first 60 s after bolus injection, and the second phase is the secretory phase in which a tracer in the blood is consistently excreted from the kidney; in 3-5 min, the tracer's concentration is expeditiously decreased. The third phase is the excretory phase in which the radioactivity decreases after its peak. The radioactivity half-life in the excretory phase is approximately 7-10 min. In the second phase, the relative renal function can be measured using the ratio of bilateral kidneys during the 1-to-2.5 min post injection period, and based on total renal function, relative renal function can be shown in ratio[8].

The measurement of the relative renal function is an important indicator for the therapeutic plan of a patient with unilateral kidney disease. Relative renal function in the range of 45%-55%, is considered normal[9].

A premise for measurement of the relative renal function is an attenuation of radioactivity between the kidney and gamma camera. If normal, 90% or more shows depth differences of 2 cm or less between the two kidneys, based on the body surface. However, with a deformity of either the spine or an ectopic kidney, it must be compensated for in-depth difference. The effective attenuation coefficient for technetium is 0.12/cm, and the linear attenuation coefficient is 0.153/cm[10]. For example, a preceding study reveals that for a kidney with 50:50 function, a 1cm difference in depth of the two kidneys shows a ratio of 53:47, whereas a 2 cm difference shows a ratio of 57:43, which signifies a shift in the functional ratio between the kidneys[11].

The kidney is a retroperitoneal organ located between the 11th thoracic vertebra and 3rd lumbar vertebra. During a renal scan using a gamma camera, the patient, generally, is in a supine position with the detector located under the table. The detector counts the gamma rays and creates an image. In the case of a transplanted kidney, the detector is located in front of the patient in a supine position for detection of gamma rays[12].

A commonly used attenuation correction software utilizes the Tonnesen equation, which is based on kidney depth data-established in non-Asians[13]. However, as the Tonnesen equation measures kidney depth using a sonography probe at a tilted angle, a precise attenuation correction is difficult. As expected, it shows the disparities associated with calculating with the detector on a supine patient in the renal scan. Moreover, since the data are based on a normal population without an unusual condition of the kidneys, there are limitations to its application on a transplanted kidney, enlarged kidney or a shrunken kidney, due to a lesion[14].

This study is based on the assumption that the depth of kidneys is different for each individual. Additionally, the kidney counting rate, acquired from the conventional method that places a detector in the back of a supine patient, may show a smaller result for more deeply located kidneys than more superficially located kidneys. This change in the depth of the kidney can be due to a renal lesion, ectopic kidney, or simultaneous possession of a transplanted kidney and own kidney. After measuring the precise depth of both kidneys in patients administered 99mTc-MAG3 by CT of the abdomen, the relative renal function ratio, acquired from the arithmetic mean of data collected with only a posterior detector, conventional kidney assessment, and relative renal function ratio (RRFR) acquired from the geometric mean of data collected with both posterior and anterior detector were compared. These measures were studied to determine the effectiveness of attenuation compensation according to the differences in the depth of the kidney.

For convenience, the difference in the depth of the two kidneys shall be phrased the kidney depth difference(KDD). Regarding the relative renal function(RRF), the difference between an RRFR calculated from the arithmetic mean acquired with only a posterior detector and an RRFR calculated from the geometric mean acquired with a posterior and anterior detector is called the RRF, difference(RRFD).

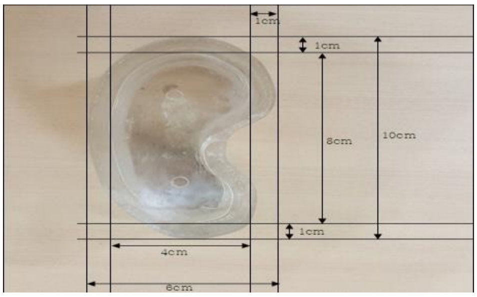
2. Method

2.1. Kidney model experiment

2.1.1. Kidney model

A kidney model was made with a 1cm thick acryl and size for a normal adult. It is 8cmx4cmx4cm internally and has a hole where the radioactive isotope can be injected <Figure 1>.

Figure 1. Kidney model.



2.1.2. Method

2.1.2.1. Change in depth of left and right kidney

On the patient examination table, an acrylic plate(25cm×25cm×1cm) was placed level. The experiment was conducted with the left and right model kidneys on the plate. Then, 20mL of 99mTc-pertechnate 2 mCi(74 Mbq) was administered into the left kidney, whereas 20mL of 99mTc-pertechnate 1.5 mCi(55.5Mbq) was administered into the right kidney. The difference in administered radioactivity signifies the difference between functions of the kidneys.

A piece of acryl(10cm×15cm×0.5cm) was placed under the right model kidney one by one, raising the height by 0.5cm, and height was raised from 0 to 0.5cm, 1cm, 1.5cm, 2cm, then 2.5cm with five acrylic plates to reflect difference in depth of the kidneys by 2.5cm.

The total height including the acrylic plates was made to be level by placing another piece of acryl on top of the left kidney when one acryl is placed under the right kidney <Figure 2>, <Figure 3>.

Figure 2. Expression of difference in depth of right and left kidneys using kidney models.

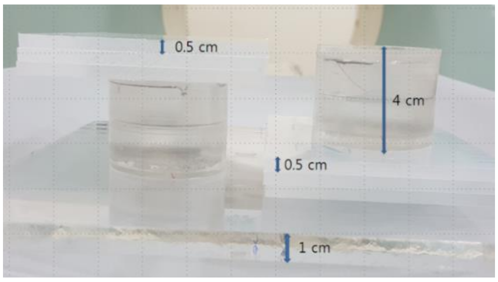
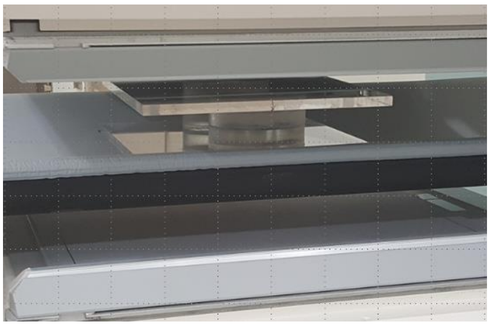


Figure 3. Radiation counting using kidney models.



2.1.2.2. Acquirement of image and calculation of relative renal function ratio

Anterior and posterior images were acquired using the Symbia T16(Siemens Healthineers, Germany) gamma camera. The matrix size was 256×256, and size of the energy window was 140 keV ± 15%, and zoom 1.45 to be calculated for 60 seconds. For confirmation of reproducibility, five images were taken at different kidney depths, for a total of 30 images.

The RRFR of the kidneys was compared with arithmetic mean using the data detected by only the posterior detector, then the, RRFR of the kidneys with geometric mean of data collected from anterior and posterior detectors.

Syngo workstation processing tool(Siemens Healthineers, Germany) was utilized. To minimize the error in establishing the region of interest(ROI), the uniform ROI was established by using a copy and paste method.

2.1.2.3. Relative renal function ratio

ROI in both kidneys is established in the renal scan image, then, total counts and pixels are measured in, which the number of pixels in ROI of kidney and ROI of background site is corrected <Figure 4>,<Figure 5>.

Figure 4. Measurement of relative renal function ratio using kidney model(arithmetic mean).

Posterior			
Parameters	ROI 1	ROI 2	Total
Split Function (%)	47.77	52.23	
Kidney Counts (cpm)	1029843	1126041	2155884

Figure 5. Measurement of relative renal function ratio using kidney model(geometric mean).

Anterior + Posterior			
Parameters	ROI 1	ROI 2	Total
Split Function (%)	53.38	46.62	
Kidney Counts (cpm)	1320233	1153271	2473504

The formula that calculates RRFR of the kidneys with data collected from the posterior detector(1) and formula hat calculates RRFR of the kidneys with geometric mean of data collected from anterior and posterior detectors(2) is as following.

(1) RRFR using arithmetic mean of posterior detector.

$$Rt = Rt \div (Rt + Lt) \times 100\ (\%)$$
$$Lt = Lt \div (Rt + Lt) \times 100\ (\%)$$

(2) RRFR using geometric mean of anterior and posterior detectors.

$$Rt = \frac{\sqrt{Rt_{ANT} \times Rt_{POST}}}{\sqrt{Rt_{ANT} \times Rt_{POST}} + \sqrt{Lt_{ANT} \times Lt_{POST}}}\ (\%)$$
$$Lt = \frac{\sqrt{Lt_{ANT} \times Lt_{POST}}}{\sqrt{Rt_{ANT} \times Rt_{POST}} + \sqrt{Lt_{ANT} \times Lt_{POST}}}\ (\%)$$

2.1.2.4. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Science software(version 23.0; SPSS Inc, USA). Linear regression analysis was performed on the influence of KDD on the difference between RRFR acquired from data calculated from posterior detector and RRFR acquired from data using geometric average of the results from anterior and posterior detectors. If the p value was less than 0.05, it was considered statistically significant.

2.2. Clinical patient study

2.2.1. Patient information

Among the patients who had undergone a 99mTc-MAG3 renal scan in our nuclear medicine department from Jan. 2015 to Dec. 2016, 57 patients(21 males, 36 females; average age, 47.08; age range, 5-70 years; average height, 160.47cm; and average weight 57.80kg) were selected as subjects.

Patients were excluded who had not undergone an abdominal CT scan or had only one kidney after surgical removal or a horseshoe kidney.

2.2.2. Experimental method

2.2.2.1. Measurement of kidney depth

The depth of the kidneys was measured based on the method proposed in a preceding study published in 2000, which was applied in this study[10].

Based on the abdominal CT images of the patients, the depths from the skin to the most anterior point of the kidney(a) and the most posterior point of the kidney(b) were measured from an image that included the renal hilum of the kidney, which was added, and divided in half to calculate kidney depth. To procure reproducibility, it was measured three times <Figure 6>.

Figure 6. Kidney depth measurement.

Note: Abdominal CT image of one of the patients, the measurement of kidney depth was obtained by adding the respective depths from skin to front and back of kidney and dividing the sum in half based on the image that depicts the renal hilum.

2.2.2.2. Acquirement of image and calculation of relative renal function ratio

The test was conducted using the Symbia T16(Siemens Healthineers, Germany) gamma camera. Anterior and posterior detectors would be closed onto the patient in supine position, with injection of 99mTc-$MAG_3$15 mCi(555 MBq).

After making a calculation with the anterior and posterior detectors, the RRFR was calculated using the data collected from the posterior detector only. Next, the RRFR was calculated with the geometric mean of the data collected from the anterior, posterior detectors. The RRFR was measured 1-2 min after the injection.

The Syngo workstation processing tool(Siemens Healthineers, Germany) was used in the measurements, and to minimize the error in establishing ROI, uniform ROI was established by using copy & paste method <Figure 7>, <Figure 8>.

Figure 7. Radiation counting.

Note: a) Radiation counting conducted with only posterior detector, which is a conventional renal test method. b) Radiation counting conducted with anterior and posterior detector for application of the geometric mean.

Figure 8. Time-activity Curve and relative renal function ratio(%) of left and right kidneys, Counts per min(cpm).

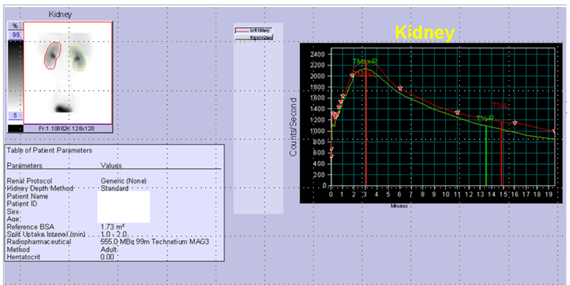


Table of Result Summary

Parameters	Left	Right	Total
Split Function (%)	51.5	48.5	
Kidney Counts (cpm)	109968	103618	213586
Time of Max (min)	3.002	3.002	
Time of ½ Max (min)	14.8	13.5	

2.2.2.3. Relative renal function ratio

ROI in the both kidneys is established in the renal scan image, then, total counts and pixels are measured, which the number of pixels in ROI of kidney and ROI of background site is corrected.

The formula that calculates RRFR of the kidneys with data collected from the posterior detector(1), and the formula that calculates RRFR of the kidneys with the geometric mean of data collected from the anterior and posterior detectors(2) is as following <Figure 9>.

(1) RRFR using arithmetic mean of posterior detector.

$$Rt = Rt \div (Rt + Lt) \times 100\ (\%)$$
$$Lt = Lt \div (Rt + Lt) \times 100\ (\%)$$

(2) RRFR using geometric mean of anterior and posterior detectors.

$$Rt = \frac{\sqrt{Rt_{ANT} \times Rt_{POST}}}{\sqrt{Rt_{ANT} \times Rt_{POST}} + \sqrt{Lt_{ANT} \times Lt_{POST}}}\ (\%)$$
$$Lt = \frac{\sqrt{Lt_{ANT} \times Lt_{POST}}}{\sqrt{Rt_{ANT} \times Rt_{POST}} + \sqrt{Lt_{ANT} \times Lt_{POST}}}\ (\%)$$

Figure 9. Application of the geometric mean.

Note: Anterior image(first row) calculated from detector 1, and posterior image(second row) calculated from detector 2, are calculated from their geometric mean to be shown in another image(third row).

2.2.2.4. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Science software(version 23.0; SPSS Inc, USA). Linear regression analysis was performed on the influence of KDD on the difference between RRFR acquired from data calculated from posterior detector and RRFR acquired from data using geometric average of the results from anterior and posterior detectors. If the p value was less than 0.05, it was considered statistically significant.

3. Results

3.1. Result of model kidney experiment

When RRFR was measured with data acquired from the posterior detector, it was an average of 51.27:48.64 if there was no difference in kidney depth. With greater KDD, RRFR would decline in the right kidney, which was located deeper. In maximum KDD of 25mm, it showed average RRFR of 62.31:37.68 <Table 1>.

Table 1. Measurements of RRFR according to the difference in kidney depth, which ranges from 0 to a maximum of 25mm(Average of five measurements in each depth difference).

	Posterior detector		Both detector	
Difference	Left	Right	Left	Right
0 mm	51.27	48.64	51.68	48.31
Right. 5 mm	55.15	44.90	53.39	46.60
Right. 10 mm	56.99	42.99	53.48	46.50
Right. 15 mm	59.00	40.98	53.37	46.61
Right. 20 mm	60.62	39.36	53.32	46.78
Right. 25 mm	62.31	37.68	53.29	46.70
Mean±SD	57.56±3.99	42.43±3.98	53.09±0.69	46.92±0.69
CV	6.93	9.38	1.29	1.47

Note: SD(Standard Deviation) / CV(Coefficient of Variation).

After comparing RRFR the using geometric mean of data collected from both anterior and posterior detectors, when there was no difference in KDD, the average was 51.68:48.31, which was not so different from the RRFR acquired from the posterior detector only. Even if KDD increased, there was little difference in RRFR when compared to that of 0 KDD.

The absolute value of KDD was set as an independent variable, and the difference between RRFR calculated from the arithmetic mean acquired with only posterior detector and RRFR calculated from geometric mean acquired with posterior and anterior detector(RRFD) was set as the dependent variable for linear regression analysis.

Regression equation between KDD and RRFD is y=0.23+0.38x, R2=0.986(p=0.000).

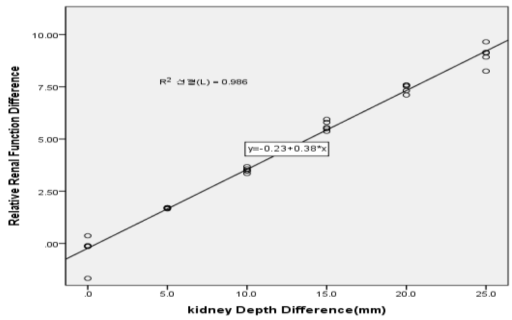
As p< 0.05, the regression model is statistically significant with R2=0.986, which changes in RRFR according to KDD and can be explained in the high standard of 98.6% <Table 2>.

Table 2. Statistics in model kidney experiment.

Variables	B	S.E	β	t	*p*	Adj-R^2	F
	.377	.008	.993	44.572	.000	.986	1986.650***

It is shown that the geometric mean of RRFR in kidneys that are located deeper increases when it is measured with anterior and posterior detectors, compared to the RRFR measured using the data collected with posterior detector as KDD increases <Figure 10>.

Figure 10. Scatter plot of model kidney experiment outcome.



3.2. Results of the clinical study

As for the depth of kidney, the left kidney was an average depth of 72.03 mm, and 78.28 mm of the right. Male showed an average depth of 81.39 mm of the left kidney and 87.06 mm of the right, whereas Female showed an average of the left kidney 66.56 mm, and 73.16 mm of the right. Both sexes showed a deeper location of the right kidney than the left, with the difference in depth of the kidneys ranging from 0.34 mm up to 60.46 mm <Table 3>.

Table 3. Average depth of the kidney in male and female.

Depth	N	Mean(mm)	SD(mm)
Left	57	72.03	20.93
Right	57	78.28	22.13
Male left	21	81.40	26.22
Male right	21	87.06	28.38
Female left	36	66.57	14.98
Female right	36	73.16	15.81

When comparing RRFR acquired from the arithmetic mean of data collected from the posterior detector with the patient in supine position to RRFR acquired from geometric mean of data collected from anterior and posterior detectors, 50 of 57 patients showed higher RRFR in the deeper-located kidney when both detectors are used rather than when only the posterior detector is used. In addition, it showed reduced RRFR in more superficial kidney.

Absolute value of KDD was set as an independent variable, and the difference between RRFR calculated from the arithmetic mean acquired with the only posterior detector and RRFR calculated from geometric mean acquired with both posterior and anterior detectors(RRFD) was set as the dependent variable for linear regression analysis <Table 4>.

Table 4. Statistical outcome of clinical experiment.

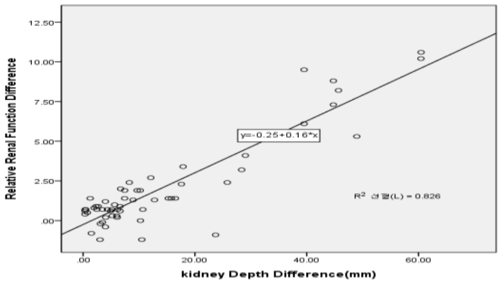
Variables	B	S.E	β	t	*p*	Adj-R^2	F
	.163	.010	.909	16.175	.000	.823	261.642***

The regression equation between KDD and RRFD was y=0.25+0.16x, R2=0.823(p=0.000).

As p< 0.05, the regression model is statistically significant with R2=0.823, which changes in RRF according to KDD can be explained in the high standard of 82.3%.

With a greater difference in KDD, RRFR of the deeper kidney was shown to be greater when it is calculated from geometric average of both anterior and posterior detectors outcomes than when calculated from the measurement of only posterior detector <Figure 11>.

Figure 11. Scatter plot of clinical experiment out- come.



4. Discussion and Conclusion

99mTc-DMSA is simple and short when comparing RRFR using the geometric mean, but in our hospital, most of the patients taking 99mTc-DMSA are infants, and it is rare for the 99mTc-DMSA scan and abdominal CT scan to be conducted simultaneously, 99mTc-MAG3 Renal Scan patients with a greater number of the experiment subjects were set as the subject for sampling.

Dynamic renal scan using 99mTc-MAG3 is a typical method of evaluating renal disease that dynamically provides continuous visualization of the process of radiopharmaceutical uptake into the kidney and its excretion.

In this study, we performed static renal scan using kidney models and dynamic renal scan using 99mTc-MAG3.

This study was a comparative analysis of the method that calculates RRFR based on Arithmetic mean of the data acquired from only posterior detector to another method that calculates RRFR based on geometric mean of the data acquired from anterior and posterior detector when conducting dynamic renal scan using 99mTc-MAG3, studying the effectiveness of applying geometric mean according to KDD.

In renal scans conducted in nuclear medicine, it is more conventional for patients in a supine position to be scanned by only the posterior detector, as. most of the population shows little difference in depth of their kidneys. However, for patients undergoing a renal scan in a hospital, they may have a higher risk of abnormality in renal function or alteration of location compared to the general population. From the outcome of this study, 23(40.35%) of 57 patients showed KDD of at least 10mm.

According to a preceding study published in 2006, 99mTc-MAG3 scan may influence RRFR when there is a difference in kidney depth[15], In addition, according to a study published in 2011, when the location of the kidney is altered by liposarcoma, RRFR calculated with only posterior detector showed RRFR of 85:15, whereas RRFR calculated with geometric mean changed up to 41:59[16].

For children with severe hydronephrosis, it was reported that more precise result could be acquired when using geometric mean in a 99mTc-DMSA scan[17]. There is also a study reporting that when there is an anatomical abnormality in the kidney, using the geometric mean in 99mTc-DMSA can result in more reliable outcomes[18].

A study argued that when conducting 99mTc-MAG3 scans of kidney donors, the conventional method and the method that uses the geometric mean show differences of up to 46% in the function ratio, thus, geometric mean must be used to heighten the precision of the renal function evaluation[19].

This study has also achieved a similar outcome as seen in preceding studies.

When there is a difference in the depth of the kidney, a renal scan performed with only a posterior detector has a disadvantage in that the attenuation of radioactivity between detector and deeply-located kidney is not reflected appropriately. However, when applying the geometric mean to the anterior and posterior detector calculation, the radiation that is discharged from the kidney that is located deeper can be counted more easily using an anterior detector, which can be considered to compensate for the reading of the posterior detector in the attenuation of relatively deeper-located kidney.

This study measured the depth of the left and right kidneys using abdominal CT image, which had not been utilized in former studies. It distinct from preceding studies that analyzed the influence in RRFR based on the image. In addition, this study has increased its credibility by supporting the outcome of the clinical experiment with model kidney experiment. However, 34 patients of 57 subject showed a difference in depth of kidneys of less than 10 mm, whereas 23 patients showed a difference of 10 mm or greater. As the measurement of kidney depth in abdominal CT image is within the range of error if the difference is minimal, the influence to RRFR would be small when the difference is minimal. Therefore, additional experiments with a greater number of samples and more distinct categories for different kidney depths would achieve more statistically balance results.

The renal scan, conducted in nuclear medicine, generally uses only posterior detector to calculate RRFR. However, when data are acquired from both anterior and posterior detector, adjusted with the geometric mean, the RRFR of a deeper-located kidney is higher than the RRFR calculated with only the posterior detector.

The results, as previously mentioned, are considered adjusted for the attenuation between kidneys that are located deeper and the detector, If there is a difference in the depth of the left and right kidneys due to a lesion in or around kidney, deformity in spine, or ectopic kidney, or in the case of a patient who received a kidney transplant and did not remove an original kidney, the kidney located deeper would compensate for its function. Therefore, when compared to a conventional scan method (posterior detector counting), a more precise calculation of kidney function is anticipated to be possible without additional cost or time consumption.

* This project was confirmed to be exempt from a review by the Institutional Review Board(IRB).

* We declare that this study is based on previous study published in 2016. In this study, We have procured additional samples and supplemented with a model kidney experiment[20].

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