RESEARCH ARTICLE

Impact of GFR Stratification on Tc-99m DTPA Dose Distribution in Target and Non-Target Organs: A MIRD-Based Comparative Study in Renogram Imaging

Luthfia Qalby*, Wahyu Setia Budi, Eko Hidayanto

Department of Physics, Faculty of Science and Mathematics, Universitas Diponegoro, Jl. Prof. Jacob Rais, Semarang 50275, Indonesia

*Corresponding author. Email: qalbyluthfia@gmail.com

Received date: Sep 29, 2025; Revised date: Oct 23, 2025; Accepted date: Oct 27, 2025

Abstract

BACKGROUND: Renogram using Technetium-99m Diethylene Triamine Pentaacetic Acid (Tc-99m DTPA) is applied to evaluate renal perfusion, glomerular filtration rate (GFR), and urinary excretion. In patients with impaired renal function, delayed tracer elimination may increase accumulation in non-target organs such as the heart and liver, resulting in greater radiation exposure and reduced image quality. Studies examining the relationship between renal function and Tc-99m DTPA dose distribution remain limited, particularly in clinical settings in Indonesia. Therefore, in this study, an organ-level quantitative analysis of Tc-99m DTPA radiopharmaceutical dose distribution and absorbed dose using the Medical Internal Radiation Dose (MIRD) approach based on Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) imaging was performed.

METHODS: Thirty adult patients undergoing renogram were categorized into low-GFR (<60 mL/min/1.73 m²) and high-GFR (≥60 mL/min/1.73 m²) groups. Each patient received 4–5 mCi of Tc-99m DTPA intravenously. Organ activities were obtained from regions of interest (ROIs) on SPECT/CT images, and organ-level absorbed doses (mGy) were calculated using the MIRD formalism.

RESULTS: In the low-GFR group, tracer retention in non-target organs increased, with absorbed doses up to twofold higher in the heart (0.0002–0.0136 mGy) and liver (0.0010–0.0178 mGy) compared to the high-GFR group. Renal absorbed doses ranged from 0.0001–0.0694 mGy, showing no significant difference between the left and right kidneys, while significant differences were observed in the heart and liver.

CONCLUSION: GFR significantly affects the radiopharmaceutical dose distribution and absorbed dose of Tc-99m DTPA. Reduced renal function increases radiation exposure in non-target organs, whereas normal function results in a more localized renal dose distribution.

KEYWORDS: Tc-99m DTPA, renogram, MIRD, glomerular filtration rate, absorbed dose, SPECT/CT, nuclear medicine

Indones Biomed J. 2025; 17(5): 503-10

Introduction

Nuclear medicine is a branch of medicine that plays a pivotal role in diagnosis and therapy of various diseases through the use of radioisotopes.(1) Among its procedures, renography is one of the most widely employed functional imaging techniques, designed to evaluate renal function comprehensively.(2) Through dynamic acquisition, renograms provide information on renal perfusion, glomerular filtration rate (GFR), and urinary excretion. (3) The procedure involves intravenous administration of a radiopharmaceutical, followed by imaging acquisition using Single Photon Emission Computed Tomography/ Computed Tomography (SPECT/CT).(4) The resulting images depict the transit of the radiopharmaceutical from systemic circulation to the kidneys and its elimination via the urinary tract.(5) Quantitative analysis of renograms

Copyright © 2025 The Prodia Education and Research Institute.
This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International (CC-BY-NC) License.

typically involves generating time–activity curves that represent perfusion, filtration, and excretory phases.(6)

Technetium-99m Diethylene Triamine Pentaacetic Acid (Tc-99m DTPA) is the most commonly used radiopharmaceutical for renography.(7) Tc-99m is derived from the natural decay of Molybdenum-99 (Mo-99), which has a half-life of approximately 66 hours.(8) This radionuclide emits gamma photons with energy of 140 keV, an ideal energy for diagnostic imaging matched to gamma camera sensitivity.(9) Its relatively short physical half-life of about 6.02 hours balances image quality with minimization of radiation dose to the patient, approximately 0.0049 mSv/MBq.(10) To target the kidneys, Tc-99m is labeled with a DTPA kit.(12) The labeling process is straightforward, rapid, and stable, producing a Tc-99m DTPA complex suitable for intravenous administration.(13)

GFR is a principal parameter in assessing renal function.(14) Estimation of GFR using serum creatinine is often inaccurate, especially in chronic kidney disease, because it is influenced by non-renal factors such as muscle mass and protein intake.(15) In contrast, Tc-99m DTPA enables a more precise estimation of GFR because the elimination of the radionuclide depends entirely on glomerular filtration.(16) Several studies have highlighted that cystatin-C offers superior sensitivity compared to serum creatinine in detecting early renal dysfunction and correlates strongly with GFR levels, particularly in obesity-related renal impairment.(17)

Although the kidneys are the primary target organs, distribution of Tc-99m DTPA is not strictly confined to renal tissue.(18) Several studies have shown that this radiopharmaceutical can accumulate in non-target organs such as the liver and heart, particularly in patients with reduced renal function.(19) A decline in GFR prolongs systemic transit time of Tc-99m DTPA, thereby increasing radiation exposure to highly perfused organs.(20) This phenomenon not only impairs renogram image quality but also carries important implications for patient radiation protection.(21)

Approximately 19–24 % of the dose absorbed by the kidneys may originate from other organs involved in the radiopharmaceutical's biokinetics, such as the liver, bladder, and surrounding tissues, particularly in individuals with impaired renal function. The renal absorbed dose of Tc-99m DTPA in adults ranged from 0.023 to 0.053 mGy/MBq, indicating a significant contribution from non-renal organs to the total body dose.(22) This suggests that at low GFR, prolonged systemic transit of Tc-99m DTPA increases the possibility of absorption and re-emission of radiation in non-target organs like the heart and liver. Consequently, this not only degrades the renogram's image quality but also elevates radiation risk to sensitive non-target organs. Moreover, Tc-99m DTPA has demonstrated superior accuracy in estimating GFR compared to creatinine-based methods, particularly in patients with chronic kidney disease.(23) Subjects with low GFR also reported to exhibit broader radiopharmaceutical distribution, leading to increased radiation dose to non-target organs.(24)

The kidney plays a central role in the excretion of radiopharmaceuticals like Tc-99m DTPA, and pathological impairments of filtration function can influence the distribution of radiation dose to both target and non-target organs. Experimental animal studies have shown that physiological factors such as hydration status and sex differences significantly affect renal clearance and susceptibility to nephrotoxicity.(25) In addition, renal dysfunction induced by ureteral obstruction or ischemia–reperfusion injury has been shown to reduce GFR.(26,27) Previous investigations have typically focused on GFR estimation or determination of effective dose in general, without taking into account how variations in renal function influence radiopharmaceutical dose distribution across organs. However, patients with low GFR are likely to retain radiopharmaceuticals more extensively, thus potentially receiving higher off-target radiation exposure. In a clinical context, understanding this phenomenon is crucial to optimizing dose protocols and enhancing patient safety in renogram procedures.

Therefore, this study was conducted to analyze the distribution and absorbed dose of Tc-99m DTPA in the target organ (kidneys) and adjacent non-target organs (heart and liver), accounting for differences in patients' GFR values. The Medical Internal Radiation Dosimetry (MIRD) approach is employed to derive quantitative estimates of inter-organ absorbed dose based on patient SPECT/CT data. This work is expected to provide deeper insights compared to previous studies by integrating GFR stratification into inter-organ dose distribution analysis, thus delivering a more comprehensive understanding of the relationship between renal function and radiation dose distribution in Tc-99m DTPA renography.

Methods

Subjects Recruitment

Thirty adult patients undergoing renogram at the Department of Nuclear Medicine, Dr. Kariadi General Hospital,

Semarang were included in this study. Inclusion criteria for subjects were: age ≥18 years, renogram with Tc-99m DTPA, GFR >15 mL/min/1.73 m², and complete imaging data. Exclusion criteria were: severe renal anatomical abnormalities, allergy to radiopharmaceuticals, end stage renal failure (GFR <15 mL/min/1.73 m²) requiring dialysis, or incomplete/poor-quality data.

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Diponegoro University (Ethical Clearance No. 168/EC/KEPK/FK-UNDIP/VII/2025) and Dr. Kariadi General Hospital, Semarang, Indonesia (Approval No. DP.04.01/ D.X/7269/2025). All procedures were conducted in accordance with the Declaration of Helsinki and relevant institutional guidelines.

Radiopharmaceutical and Administration Protocol

All renogram examinations were performed using Tc-99m DTPA as the radiopharmaceutical. An activity of 4–5 mCi (148–185 MBq) was intravenously administered in accordance with the standard clinical protocol of the Department of Nuclear Medicine, Dr. Kariadi General Hospital, Semarang. The administered activity was adjusted according to each subject's body weight and age to ensure optimal image quality while maintaining radiation safety.

The Determination of Regions of interests (ROI)

Immediately following intravenous injection, dynamic images were acquired for 15–20 minutes using a SPECT/CT Discovery NM/CT 670 system (GE Healthcare, Chicago, IL, USA). The acquired images were initially processed on the Processing Station and subsequently transferred to the Xeleris 4 workstation (GE Healthcare) for advanced analysis.

Subject's GFR values derived from imaging were used to classify subjects into two groups, based on the criteria for adult renal function (normal GFR ≈120 mL/min/1.73 m²): low-GFR group, with GFR<60 mL/min/1.73 m² (indicating abnormal renal function); and high-GFR group, with GFR≥60 mL/min/1.73 m² (indicating normal renal function).(28)

Regions of interests (ROIs) were defined during the uptake phase, as Tc-99m DTPA accumulates optimally within the renal parenchyma proportional to GFR, with minimal contribution from blood and the pelvicalyceal system. Therefore, the uptake phase most accurately represents the actual renal function compared to the early or late phases.(29) ROIs were defined for both the target organs and surrounding tissues. For kidneys, the ROIs were determined semi-automatically using the Renal Analysis feature in Xeleris 4. The system assisted in delineating renal boundaries consistently, although the operator could manually adjust ROI placement when image quality was suboptimal. Meanwhile, for the adjacent organs (heart and liver), after saving the Renal Analysis results, ROIs for adjacent organs were manually delineated using the Load to New function in Xeleris 4.

Estimation of Tc-99m DTPA Absorbed Dose

Normalization calibration of uptake was performed using the built-in Renal Analysis method with Rutland plots background subtraction. A correction factor was obtained from scanning a syringe containing 1 mCi Tc-99m DTPA positioned identically to subject scans. The syringe image was analyzed with a corresponding background ROI, yielding a correction factor of 0.000371 mCi/cps. From each ROI, the total counts of Tc-99m DTPA accumulated within the organ were obtained. These count values were used to calculate the relative activity uptake distribution across organs, which served as the basis for absorbed dose estimation.

Dosimetric Analysis Using MIRD Formalism

Data processing in this study was performed using the MIRD formalism to estimate the absorbed dose distribution in both target and surrounding organs. The analytical procedure consisted of several sequential steps. First, the ROI was delineated semi-automatically using Xeleris 4 software (GE Healthcare) on dynamic renogram images. The ROI included the target organ (kidney) and adjacent organs (liver and heart), which were clearly visualized during the dynamic acquisition sequence.

The radiopharmaceutical activity in each organ was determined from the proportion of counts obtained within the ROI, multiplied by the administered activity (A_0) and the system calibration factor (F_K), expressed as A (mCi) = (count) × F_K (mCi/count). The percentage uptake for each organ was then calculated by comparing the measured organ activity (A) to the administered activity (A_0) and multiplying by 100%, *i.e.*, so that the % uptake = $(A/A_0) \times 100\%$.

The effective activity ($\tilde{A}$), representing the time-integrated activity within an organ, was subsequently obtained by multiplying the organ activity with its residence time (τ), formulated as $\tilde{A} = A \times \tau$. In renogram studies, quantitative parameters such as time-to-peak and clearance half-time ($t_{1/2}$) are commonly employed to assess renal function and tracer excretion efficiency.(30) These parameters reflect renal clearance dynamics and serve

as indicators for evaluating renal performance.(31) In this study, the residence time (τ) was used as a surrogate parameter to represent tracer clearance from the kidney, based on its conceptual equivalence to temporal indices such as time-to-peak and $t_{1/2}$, both describing the kinetic behavior of radiopharmaceutical excretion.

The S-value, which represents the absorbed dose per unit of effective activity, was adopted from previous study.(32) Finally, the absorbed dose (D) for each organ was calculated as the product of the effective activity and the corresponding S-value, expressed as $D = \tilde{A} \times S$. The resulting values represented the absorbed dose (mGy) received by each organ during the renogram procedure, which were subsequently analyzed to evaluate radiation distribution and potential risk to the kidneys and adjacent tissues.

Results

Subjects Characteristics

A total of 30 data from included subjects were analyzed, including 15 with low GFR (<60 mL/min/1.73 m²) and 15 with high GFR (≥60 mL/min/1.73 m²). The injected activity of Tc-99m DTPA ranged from 4–5 mCi. Overall, subjects with low GFR demonstrated markedly greater redistribution of Tc-99m DTPA to non-target organs such as the liver and heart, accompanied by up to a twofold increase in absorbed dose compared to the high-GFR group. This finding was clinically relevant, as it implies higher non-target exposure and potentially reduced image quality in renogram studies of subjects with impaired renal function.

Baseline characteristics of both groups were summarized in Table 1, showing significant differences in mean GFR and age between the two groups (p<0.001). These differences serve as the foundation for analyzing variations in tracer uptake and absorbed dose across organs.

Radiopharmaceutical Activity Uptake Distribution

In subjects with low GFR, the mean renal uptake ranged from 17.1–20.5%, whereas uptake by the heart and liver increased to 25.0% and 37.4%, respectively. In contrast, the high-GFR group exhibited higher renal uptake 25.4–28.4% and reduced uptake in the heart 18.7% and liver 27.5%. These findings indicate that impaired renal filtration promotes radiopharmaceutical redistribution toward non-target organs due to delayed tracer clearance and secondary hepatic retention.

Organ Dose Distribution of Tc-99m DTPA in Low- and High-GFR Groups

Absorbed dose calculations using the MIRD formalism revealed distinct distribution patterns between the two groups (Figure 1). In the low-GFR group, absorbed doses were 0.0001–0.0694 mGy in the kidneys, 0.0002–0.0136 mGy in the heart, and 0.0010–0.0178 mGy in the liver. In the high-GFR group, renal doses were higher (0.0023–0.0343 mGy), while cardiac and hepatic doses were lower, 0.0001–0.0016 mGy and 0.0004–0.00465 mGy, respectively.

The mean uptake and absorbed dose percentages was presented in Table 2. Despite higher renal doses in subjcts with normal function, non-target organs received substantially lower radiation exposure. This redistribution of absorbed dose also affected image quality. As shown in Figure 1A, subjects with low GFR exhibited poor contrast due to intense non-target activity that caused scatter and spillover, masking renal signals. Conversely, Figure 1B demonstrated that high-GFR subjects produced higher-contrast images, facilitating clearer ROI delineation and functional interpretation. Although renal doses were higher in high GFR subjects, non-target organs received relatively lower doses. Absorbed dose distribution is influenced not only by uptake but also by retention time and organ perfusion.

Organ Dose Variation and Renogram Pattern Differences Between GFR Groups

Inferential statistical testing using independent t-tests was performed to compare absorbed doses between the two GFR groups (Table 3). Significant differences were observed in non-target organs (heart and liver), while renal doses did not differ significantly, aligning with the expected

Table 1. Characteristics of study subjects.

Groups	Age (Years)	GFR Value (mL/minutes/1.73 m^3)	Renal Function Category
	Mean±SD	Mean±SD	
Low GFR	54.53±14.46	32.71±10.5	Abnormal
High GFR	45.93±12.42	86.88±17.54	Normal

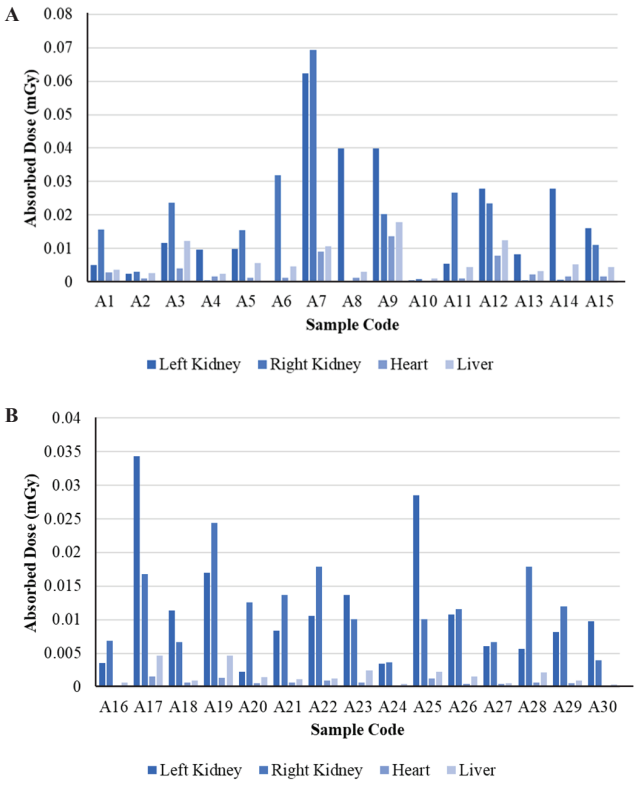

Figure 1. Absorbed dose values of Tc-99m DTPA in subjects. A: Subjects with low GFR. B: Subjects with high GFR.

radiopharmaceutical dose distribution of Tc-99m DTPA as a glomerular filtration tracer. These findings emphasize that impaired renal function increases radiation exposure to non-target organs, underscoring the need for dose and timing adjustment in renogram imaging to minimize unnecessary exposure.

Time–Activity Curve Analysis

The renal time–activity curves revealed clear distinctions between normal and impaired kidney function. In the low-GFR group, the renogram curve showed a delayed peak and slow decline, indicating impaired tracer excretion and prolonged retention. In contrast, subjects with high GFR exhibited an earlier peak and a steeper washout phase, consistent with efficient glomerular filtration.

Representative subject analysis demonstrated the classic three-phase pattern (perfusion, parenchymal uptake, and excretion) in the high-GFR group, with normal time-to-peak (T_{max}), half-time ($T_{1/2}$), and a 30-min/peak ratio <0.8. Meanwhile, in the low-GFR group, although parenchymal uptake remained visible, the excretory phase was markedly delayed, producing a flatter curve and a 30-min/peak ratio >0.8, indicative of tracer retention and excretory dysfunction (Figure 2).

These curve differences highlight that Tc-99m DTPA not only reflects glomerular filtration rate but also visualizes tracer redistribution to non-target organs under impaired renal function, serving as a sensitive indicator of both renal dysfunction and altered tracer kinetics.

Discussion

This study demonstrates that renal function status markedly influences the radiopharmaceutical dose distribution and internal dose of Tc-99m DTPA. Patients with high GFR exhibited renogram curves consistent with efficient glomerular filtration, whereas patients with low GFR showed delayed peaks and prolonged clearance. These physiological differences resulted in greater radiopharmaceutical retention in non-target organs, particularly the liver and heart, and revealed distinct absorbed-dose distributions based on MIRD analysis. In patients with reduced renal function, Tc-99m DTPA remained in circulation for a longer duration, thereby increasing exposure to highly perfused organs such as the heart and liver.(33) This redistribution is consistent with the compensatory clearance phenomenon, in which non-target organs act as secondary transit pathways when renal elimination is impaired.(34)

The observed pattern indicates that the radiation burden shifts toward the heart and liver under impaired renal function, consistent with previous findings reporting that tracer retention and hepatobiliary involvement under reduced renal clearance conditions.(10) Similar image degradation mechanisms were also linked increased extra-

Table 2. Mean uptake and absorbed dose percentage of Tc-99m DTPA.

Parameter (%)	Group	Left Kidney	Right Kidney	Heart	Liver
Uptake (%)	Low GFR	17.1%	20.5%	25%	37.4%
	High GFR	28.4%	25.4%	18.7%	27.5%
Absorbed Dose (%)	Low GFR	40.8%	37.2%	7.8%	14.3%
	High GFR	45.1%	45.4%	2.8%	6.8%

Table 3. Statistical comparison of absorbed doses.

Organ	*p*-value	Significance
Left Kidney	0.2500	Not significant
Right Kidney	0.3800	Not significant
Heart	0.0180	Significant
Liver	0.0035	Significant

renal activity with reduced renogram accuracy.(34) Greater activity in non-target organs among low GFR patients reflects slower clearance, with temporary storage in the heart and liver.(35) The observed liver uptake supports an alternative hepatobiliary excretion pathway that becomes more prominent when renal function is impaired.(36) Conversely, in high GFR patients, most of the tracer was promptly filtered and eliminated by the kidneys, resulting in steeper washout curves and more localized absorbed doses. (37) These findings emphasize that renal function directly affects time–activity profiles, organ exposure, and absorbed dose patterns, which are crucial for optimizing renogram acquisition protocols.(2)

The altered distribution can be explained by the elimination physiology of Tc-99m DTPA, which is almost entirely excreted through glomerular filtration without significant metabolism. In high-GFR patients, the tracer was rapidly filtered and eliminated by the kidneys, producing higher absorbed doses in the target organ and improved image quality.(2) Conversely, in low-GFR patients, the tracer persisted longer in the systemic circulation and accumulated in highly perfused organs.(38) The liver likely represents an alternative excretion pathway via the hepatobiliary route (39), while the heart is exposed due to continuous myocardial blood flow.(33) This mechanism accounts for the increased uptake and absorbed dose in non-target organs observed in the low GFR group.

These findings confirm that absorbed dose distribution is determined not only by organ uptake but also by retention time, perfusion, and organ mass.(34) In low GFR patients, cumulative exposure to non-target organs, although relatively low in absolute terms, may become clinically relevant with repeated examinations. In high GFR patients, concentration of the tracer in the kidneys

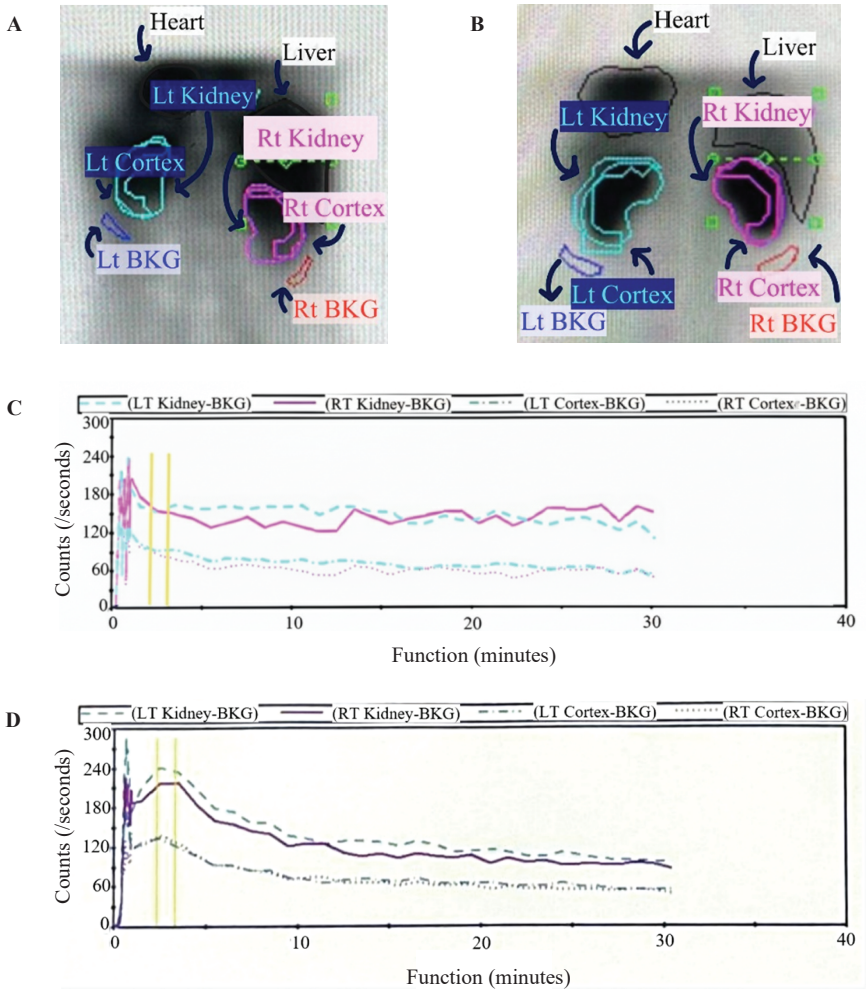

Figure 2. Representative renogram images and renogram curves of subjects. A: Renogram image of low GFR subject. B: Renogram image of high GFR subject. C: renogram curve of low GFR subject. D: renogram curve of high GFR subject. Lt = left; Rt = right; Kidney = renal parenchyma; Cortex = renal cortical region; BKG = background region; Heart = cardiac ROI; Liver = hepatic ROI.

improves image quality but also increases the absorbed dose to the target organ. These results are critical for optimizing injected activity, scatter correction, and acquisition timing in renogram procedures to enhance image quality while maintaining patient safety.

Importantly, this work addresses a knowledge gap in the Indonesian population, where quantitative data on Tc-99m DTPA dose distribution in non-target organs remain limited. Previous studies of renal radiopharmaceuticals have primarily focused on target organ kinetics or used surrogate dosimetry models without direct uptake measurement. By applying a patient-specific, MIRD-based approach to both kidneys and non-target organs, this study provides new evidence on how renal impairment alters radiopharmaceutical dose distribution.

This analysis also underscores the importance of personalizing renogram protocols according to renal function. Adjusting radiopharmaceutical activity and acquisition strategies can improve diagnostic reliability while minimizing non-target exposure, in accordance with radiation protection principles. Compared with other renal tracers such as Tc-99m MAG3 and Tc-99m DMSA, Tc-99m DTPA offers the highest specificity for glomerular filtration, making it particularly suitable for quantitative GFR assessment.(40) The present findings reinforce Tc-99m DTPA's role as a reference tracer and demonstrate that MIRD-based dosimetry can enhance its diagnostic and safety profile in nuclear medicine practice. A limitation of this study is the absence of inferential statistical analyses; therefore, future research with larger sample sizes is recommended to enable hypothesis testing and confirm the observed trends.

Conclusion

The result of this study demonstrates that the distribution and absorbed dose of Tc-99m DTPA in renogram procedures are strongly influenced by the patient's GFR. Tc-99m DTPA accumulates not only in the kidneys as the target organ but also in non-target organs such as the heart and liver. In patients with low GFR, renal uptake is lower and more variable, while non-target organs receive higher uptake and absorbed doses due to delayed renal elimination. Conversely, in patients with high GFR, the radiopharmaceutical distribution is more localized in the kidneys, resulting in better data quality but with a relatively higher absorbed dose in the kidneys compared to non-target organs.

Acknowledgments

The author would like to thank the Department of Nuclear Medicine, Dr. Kariadi General Hospital, Semarang, for providing the facilities and access to renogram data that made this study possible.

Authors Contribution

LQ conceived and designed the study, performed data collection, analysis, and interpretation, and drafted the manuscript; WSB provided guidance on study design, supervised data analysis, and critically revised the manuscript; EH assisted with technical supervision, interpretation of results, and manuscript revision. All authors read and approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflict of interest regarding the research and publication of this article. This research was conducted independently without external funding.

References

1. Roy I, Krishnan S, Kabashin AV, Zavestovskaya IN, Prasad PN. Transforming nuclear medicine with nanoradiopharmaceuticals. ACS Nano. 2022; 16(4): 5036–61.
2. Fried JG, Morgan MA. Renal imaging: Core curriculum 2019. Am J Kidney Dis. 2019; 73(4): 552–65.
3. Zheng MM, Zhu YC, Shang LM, Du CK, Zhang L, Sun W, *et al.* Use of CT-based renal volumetry for the measurement of split renal function: a split glomerular filtration rate prediction model based on unilateral renal volume parameters. Clin Radiol. 2022; 77(10): 759–66.
4. Chiriac IA, Mititelu RM, Mazilu C, Niculescu O, Lepuș MG. Scintigraphic evaluation of the kidney. Rom J Mil Med. 2015; 118: 26–32.
5. Szabo Z, Alachkar N, Xia J, Mathews WB, Rabb H. Molecular imaging of the kidneys. Semin Nucl Med. 2011; 41(1): 20–8.
6. Farmelant MH, Burrows BA. The renogram: Physiologic basis and current clinical use. Semin Nucl Med. 1974; 4(1): 61–73.
7. Misbah TA, Chowdhury AM. Evaluation of renal function after pyeloplasty determined by 99mTc DTPA renogram. Birdem Med J. 2022; 12(2): 142–6.
8. Boschi A, Martini P, Pasquali M, Uccelli L. Recent achievements in Tc-99m radiopharmaceutical direct production by medical cyclotrons. Drug Dev Ind Pharm. 2017; 43(9): 1402–12.
9. Dendooven P, Bubba TA. Gamma ray emission imaging in the medical and nuclear safeguards fields. In: Lenzi SM, Cortina-Gil D,

editors. The Euroschool on Exotic Beams, Vol. VI. Lecture Notes in Physics 1005. Heidelberg: Springer Berlin; 2022. p.245–95.
10. Warwick J, Holness J. Measurement of Glomerular Filtration Rate. Semin Nucl Med. 2022; 52(4): 453–66.
11. Boschi A, Uccelli L, Martini P. A picture of modern Tc-99m radiopharmaceuticals: Production, chemistry, and applications in molecular imaging. Applied Sciences. 2019; 9(12): 2526. doi: 10.3390/app9122526.
12. Hossain A, Islam B, Ckaki CK, Shaha SK, Chowdhury SI. The estimation of glomerular filtration rate (GFR) for renal split function with 99m Tc-DTPA. J Adv Res Appl Sci. 2015; 2(11): 10–8.
13. Akbar MU, Ahmad MR, Shaheen A, Mushtaq S. A review on evaluation of technetium-99m labeled radiopharmaceuticals. J Radioanal Nucl Chem. 2016; 310(2): 477–93.
14. Delanaye P, White CA, Ebert N, Rule AD. Assessing kidney function. In: Chronic Renal Disease. Elsevier; 2020. p. 37–54.
15. Zsom L, Zsom M, Salim SA, Fülöp T. Estimated glomerular filtration rate in chronic kidney disease: a critical review of estimate-based predictions of individual outcomes in kidney disease. Toxins. 2022; 14(2): 127. doi: 10.3390/toxins14020127.
16. Rathmann SM, Ahmad Z, Slikboer S, Bilton HA, Snider DP, Valliant JF. The radiopharmaceutical chemistry of technetium-99m. In: Radiopharmaceutical Chemistry. Gewerbestrasse: Springer Nature Switzerland; 2019. p.311–33.
17. Ridwan R, Febriza A, Linggi EB, Natzir R, Tazlim NA. Correlation between blood pressure and obesity parameter against cystatin-C and adiponectin levels in serum of obese adolescent. Mol Cell Biomed Sci. 2020; 4(3): 105–12.
18. Keramida G, James JM, Prescott MC, Peters AM. Pitfalls and limitations of radionuclide renal imaging in adults. Semin Nucl Med. 2015; 45(5): 428–39.
19. Ahmed N, Zia M. Diagnostic modalities and radiopharmaceuticals with particular importance of technetium-99m (99mTc). Chin J Acad Radiol. 2023; 6(4): 143–59.
20. Komal S, Nadeem S, Faheem Z, Raza A, Sarwer K, Umer H, *et al.* Localization mechanisms of radiopharmaceuticals. In: Naqvi SAR, Imrani MB. Medical Isotopes. London: IntechOpen; 2020. doi: 10.5772/intechopen.94099.
21. Elmore JM, Cerwinka WH, Kirsch AJ. Assessment of renal obstructive disorders: Ultrasound, nuclear medicine, and magnetic resonance imaging. In: The Kelalis King Belman Textbook of Clinical Pediatric Urology. Boca Raton: CRC Press; 2018. p. 495–504.
22. Arteaga MV, Caballero VM, Rengifo KM. Dosimetry of 99m Tc (DTPA, DMSA and MAG3) used in renal function studies of newborns and children. Appl Radiat Isot. 2018; 138: 25–8.
23. Li R, Jia Y, Yi X, Wang L, Huang Q. Evaluation of six GFR estimation equations in Chinese patients with chronic kidney disease. Clin Chim Acta. 2025: 575: 120374. doi: 10.1016/j.cca.2025.120374.
24. Schreuder N, de Romijn I, Jager PL, Kosterink JG, van Puijenbroek EP. Safe use of radiopharmaceuticals in patients with chronic kidney disease: a systematic review. EJNMMI Radiopharm Chem. 2021; 6(1): 27. doi: 10.1186/s41181-021-00145-w.
25. Karimi F, Kasaei S, Baradaran A, Ashrafi F, Talebi A, Lak Z, *et al.* Dextrose hydration may promote cisplatin-induced nephrotoxicity in rats: gender-related difference. Indones Biomed J. 2019; 11(2): 136–44.
26. Lak Z, Vahdati A, Nematbakhsh M. The effect of estradiol on renal function in reversible and irreversible unilateral ureteral obstruction in rats. Indones Biomed J. 2018; 10(3): 263–9.
27. Cahyawati PN, Lestari DPO, Siskayani AS, Ariawan IMT. Simvastatin improves renal function and glomerulosclerosis in ischemic-reperfusion injury. Indones Biomed J. 2020; 12(2): 143–8.
28. National Kidney Foundation [Internet]. Estimated Glomerular Filtration Rate (eGFR) [updated 2022 Jul 13; cited 2025 Aug 10]. Available from: https://www.kidney.org/kidney-topics/estimated-glomerular-filtration-rate-egfr.
29. Taylor AT. Radionuclides in nephrourology, part 1: Radiopharmaceuticals, quality control, and quantitative indices. J Nucl Med. 2014; 55(4): 608–15.
30. Taylor A. Radionuclide renography: a personal approach. Semin Nucl Med. 1999; 29(2): 102–27.
31. Prigent A, Cosgriff P, Gates GF, Graneurs G, Fine EJ, Itoh K, *et al.* Consensus report on quality control of quantitative measurements of renal function obtained from the renogram: International Consensus Committee from the Scientific Committee of Radionuclides in Nephrourology. Semin Nucl Med. 1999; 29(2): 146–59.
32. Mattsson S, Johansson L, Leide Svegborn S, Liniecki J, Noßke D, Riklund KÅ, *et al*. ICRP Publication 128: Radiation dose to patients from radiopharmaceuticals: A compendium of current information related to frequently used substances. Ann ICRP. 2015; 44(Suppl 2): 7–321.
33. Boschi A, Uccelli L, Marvelli L, Cittanti C, Giganti M, Martini P. Technetium-99m radiopharmaceuticals for ideal myocardial perfusion imaging: Lost and found opportunities. Molecules. 2022; 27(4): 1188. doi: 10.3390/molecules27041188.
34. Sallam M, Nguyen NT, Sainsbury F, Kimizuka N, Muyldermans S, Benešová-Schäfer M. PSMA-targeted radiotheranostics in modern nuclear medicine: Then, now, and what of the future? Theranostics. 2024; 14(8): 3043–79.
35. Bolch WE, Eckerman KF, Sgouros G, Thomas SR. MIRD pamphlet no. 21: A generalized schema for radiopharmaceutical dosimetry—standardization of nomenclature. J Nucl Med. 2009; 50(3): 477–84.
36. Droździk M, Oswald S, Droździk A. Extrahepatic drug transporters in liver failure: Focus on kidney and gastrointestinal tract. Int J Mol Sci. 2020; 21(16): 5737. doi: 10.3390/ijms21165737.
37. Svensson J, Berg G, Wängberg B, Larsson M, Forssell-Aronsson E, Bernhardt P. Renal function affects absorbed dose to the kidneys and haematological toxicity during 177Lu-DOTATATE treatment. Eur J Nucl Med Mol Imaging. 2015; 42(6): 947–55.
38. Leatherby RJ, Theodorou C, Dhanda R. Renal physiology: Blood flow, glomerular filtration and plasma clearance. Anaesth Intensive Care Med. 2021; 22(7): 439–42.
39. Fritzberg AR, Klingensmith WC, Whitney WP, Kuni CC. Chemical and biological studies of Tc-99m N, N′-bis (mercaptoacetamido) ethylenediamine: A potential replacement for I-131 iodohippurate. J Nucl Med. 1981; 22(3): 258–63.
40. Schwartz GJ. Clinical assessment of renal function. In: Clinical Pediatric Nephrology. Boca Raton: CRC Press; 2016. p. 61–88.