RESEARCH ARTICLE
Araştırma Makalesi

Correspondence address
Yazışma adresi
Armagan AYDIN
Istanbul Kent University,
Vocational School of Health Service,
Istanbul, Türkiye

armanaydin@gmail.com

Geliş tarihi / *Received* : September 20, 2024
Kabul Tarihi / *Accepted* : March 26, 2025

Cite this article as
Bu makalede yapılacak atıf
Aydin A, Yeyin N, Demir M.
Assessment of Renal Dosimetry and Nephrotoxicity in Patients with Neuroendocrine Tumors Treated with 177Lu-DOTATATE

Akd Med J 2025;11(3): 444-451

Armagan AYDIN
Istanbul Kent University,
Vocational School of Health Service,
Istanbul, Türkiye

Nami YEYIN
Department of Nuclear Medicine,
Cerrahpaşa Faculty of Medicine,
Istanbul University Cerrahpaşa,
Istanbul, Türkiye

Mustafa DEMIR
Department of Nuclear Medicine, Cerrahpaşa Faculty of Medicine, Istanbul University Cerrahpaşa, Istanbul, Türkiye

Assessment of Renal Dosimetry and Nephrotoxicity in Patients with Neuroendocrine Tumors Treated with ^{177}Lu-DOTATATE

^{177}Lu-DOTATATE ile Tedavi Edilen Nöroendokrin Tümörlü Hastalarda Renal Dozimetri ve Nefrotoksisite Değerlendirmesi

ABSTRACT

Objective

This study aimed to conduct dosimetry and evaluate renal toxicity based on calculated kidney doses and glomerular filtration rates (GFR) in 22 patients diagnosed with neuroendocrine tumors following the administration of 5550 MBq (150 mCi) of ^{177}Lu-DOTATATE radiopharmaceutical.

Materials and Methods

Patients, aged between 35 and 80, including 14 males and 8 females, underwent ^{68}Ga-DOTATATE PET/CT scans to identify lesions and subsequently received treatment planning. Dosimetry of ^{177}Lu-DOTATATE was performed using whole-body imaging based on scans acquired at 4, 24, 48, and 72 hours post-administration.

Results

According to our results, the average number of treatment cycles was 5±1, with an average total kidney dose of 24.32±3.5 (Gy), average total BED dose of 27.9±2.5 (Gy), average whole-body dose of 1.83±0.4 (Gy), and average GFR of 69.95±12.2. The correlation between kidney doses and GFR was calculated as $R^2=0.7945$. The significance of the relationship between total kidney doses and total kidney BED doses was evaluated using the Mann-Whitney U test ($p=0.0244$).

Conclusion

The study found that as the number of treatment cycles increased, the total kidney dose also increased; however, rapid declines in GFR were not observed, and none of the treated patients reached toxic doses in the kidneys.

Key Words

MIRD method, ^{68}Ga-DOTATATE, ^{177}Lu-DOTATATE, Neuroendocrine tumor, Radionuclide dosimetry

DOI: 10.53394/akd.1553427

ÖZ

Amaç

Bu çalışmanın amacı, nöroendokrin tümör tanısı almış 22 hastada, 5550 MBq (150 mCi) ^{177}Lu-DOTATATE radyofarmasötik uygulaması sonrasında hesaplanan böbrek dozları ve glomerüler filtrasyon hızlarına (GFR) dayalı olarak dozimetri yapmak ve renal toksisiteyi değerlendirmektir.

Gereç ve Yöntemler

Otuz beş ile 80 yaşları arasında, 14 erkek ve 8 kadından oluşan hastalar, lezyonları belirlemek için ^{68}Ga-DOTATATE PET/CT taramaları geçirmiş ve ardından tedavi planlaması yapılmıştır. ^{177}Lu-DOTATATE dozimetrisi, uygulamadan sonraki 4, 24, 48 ve 72. saatlerde elde edilen taramalara dayalı olarak tüm vücut görüntüleme kullanılarak yapıldı.

Bulgular

Sonuçlarımıza göre, ortalama tedavi döngüsü sayısı 5±1, ortalama toplam böbrek dozu 24,32±3,5 (Gy), ortalama toplam BED dozu 27,9±2,5 (Gy), ortalama tüm vücut dozu 1,83±0,4 (Gy) ve ortalama GFR 69,95±12,2 olarak bulunmuştur. Böbrek dozları ile GFR arasındaki korelasyon $R^2=0,7945$ olarak hesaplanmıştır. Toplam böbrek dozsları ile toplam böbrek BED dozları arasındaki ilişkinin anlamlılığı Mann-Whitney U testi kullanılarak değerlendirilmiştir (p=0,0244).

Sonuç

Çalışma, tedavi döngüsü sayısı arttıkça toplam böbrek dozunun da arttığını; ancak GFR'de hızlı düşüşlerin gözlemlenmediğini ve tedavi edilen hastaların hiçbirinin böbreklerde toksik dozlara ulaşmadığını bulmuştur.

Anahtar Kelimeler

MIRD metodu, ^{68}Ga DOTATATE, ^{177}Lu DOTATATE, Nöroendokrin tümör, Radyonüklit dozimetri

INTRODUCTION

Peptide receptor radionuclide therapy (PRRT), utilizing ^{177}Lu-labeled DOTATATE with somatostatin analogs, stands out as an effective treatment method for neuroendocrine tumors (1). While generally well-tolerated, PRRT poses a critical consideration for dose tolerance in the kidneys due to the active reabsorption of the radionuclide-labeled somatostatin analog. It is acknowledged that, depending on individual patient variations, the administered activity of ^{177}Lu DOTATATE can reach toxic levels for the kidneys and bone marrow (2).

Three different dosimetric approaches are feasible in ^{177}Lu-labeled peptide therapies: organ dosimetry, bone marrow dosimetry, and lesion dosimetry. The fundamental basis for these dosimetric approaches typically involves the use of the Medical Internal Radiation Dose (MIRD) method (3). Through this method, predetermined doses to tumors, critical organs, and the whole body are established, guiding treatment planning accordingly. Kidney dose is generally considered a crucial parameter in radionuclide therapies. However, when evaluating renal toxicity, considering both the absorbed dose to the kidneys and the Biological Effective Dose (BED) for the kidneys and the entire body becomes more meaningful. The renal absorbed dose tolerance is reported as 23 Gy in external beam therapies. Some studies have calculated BED by adapting a specific linear-quadratic model for radionuclide therapy. Moreover, for patients without risk factors for renal toxicity, a safe renal absorbed dose limit of approximately 40 Gy in ^{177}Lu DOTATATE therapy has been determined, while for patients with specific risk factors, including hypertension, diabetes mellitus, and impaired renal function, BED has been established as 28 Gy (4). Gupta and colleagues have reported that patients are affected to varying degrees based on renal function, with PRRT causing more toxic effects in patients with lower GFR (5). Through dosimetric calculations, determining the precise therapeutic activity of ^{177}Lu, comparing it with renal tolerance values, and ensuring that the administered activity remains below defined limits can be achieved.

The objective of this study is to conduct dosimetry in ^{177}Lu DOTATATE therapy, determine the relationship between absorbed dose and BED, and investigate the levels of GFR impact based on the administered ^{177}Lu activity.

MATERIAL and METHODS

Ethical Approval: Ethical approval for this study was obtained from the Istanbul University Cerrahpasa Faculty of Medicine Clinical Research Ethics Committee (Document number: 83045809/604/5855). Twenty-two patients undergoing neuroendocrine tumor treatment at the Department of Nuclear Medicine, Cerrahpasa Faculty of Medicine, Istanbul University, were included in this study. The patients, consisting of 14 males and 8 females with ages ranging from 35 to 80 (mean age 67), underwent ^{68}Ga DOTATATE PET/CT imaging to identify lesions.

Treatment planning was conducted for these patients, and dosimetry was performed following the intravenous infusion of 5550 MBq (150 mCi) of ^{177}Lu DOTATATE. Prior to the commencement of the study, patients were informed about the diagnostic and treatment procedures, and written consent was obtained from each participant.

Scintigraphic Imaging: ^{68s}Ga DOTATATE PET/CT imaging was conducted using the Siemens Horizon Biograph PET/CT system. Image processing utilized the ordered subset expectation maximization (OSEM) reconstruction algorithm, including time-of-flight (TOF), scatter correction, attenuation correction, dead-time correction, random correction, and no post-reconstruction filtering. The reconstruction involved 16 subsets with 4 iterations, resulting in a voxel size of $4.1 \times 4.1 \times 3.0$ mm³.

Whole-body imaging for ^{177}Lu-DOTATATE was performed at 4, 24, 48, and 72 hours post-administration using Siemens Symbia T16 SPECT/CT with medium-energy parallel-hole collimators and a 15% energy window. Organs of interest included kidneys, liver, spleen, bone marrow, and the rest of the body. Cumulative activities for all organs except bone marrow were calculated using anterior and posterior whole-body images acquired at 4, 24, 48, and 72 hours post-injection. Region of interest (ROI) counts were utilized for cumulative activity calculations. To preserve the kidneys during treatments, a 4-hour amino acid infusion was initiated half an hour before the radiopharmaceutical injection.

Absorbed Dose Calculation

Absorbed doses were calculated using the Medical Internal Radiation Dosimetry (MIRD) method. Formula (1) was employed for absorbed dose (D) calculations (6, 7).

$$D(r_T, T_D) = \sum_{r_s} \int_0^{T_D} A(r_S, t) S(r_T \leftarrow r_S, t) dt \quad \text{.................................(1)}$$

Here, $D(r_T, TD)$ represents the absorbed dose, $A(r_S, t)$ is the cumulative activity of the radiopharmaceutical in tissue r_S at time t, and $S(r_T \leftarrow r_S, t)$ is the dose delivered from source organ r_S to target organ r_T during time t.

The total counts for the source organ in the scintigraphic images were determined using the geometric background subtraction method, as defined in MIRD Handbook No. 16 (8).This formulation is expressed by equation (2).

$$A_k = \sqrt{\frac{I_A I_P}{e^{-\mu_e t}}} \frac{f_k}{C} F_k \quad \text{...(2)}$$

Here, A_k is the cumulative activity, I_A and I_P are the anterior and posterior counts, F_k is the ^{177}Lu attenuation correction factor, μe is the linear attenuation coefficient, t is the time, C is the gamma camera calibration factor, f_k is the posterior background counts.

In the MIRD formalism, the absorbed dose D (Gy) is defined as the product of the cumulated activity and the S-value. In the dosimetry of ^{177}Lu-DOTATATE, lesion-based dosimetry is applied to calculate tumor doses. In lesion-based dosimetry, the cumulated activity is determined according to the equation provided in Equation (2). The selection of the S-value depends on the mass of the lesion. Separate S-value tables have been established for male and female patients based on MIRD phantoms. Therefore, the appropriate S-value can be selected according to the patient's sex and the mass of the lesion. For instance, the S-value for a 100-gram kidney in an adult male has been determined as 4.65×10^{-3} rad/μCi·hour (9).

Counts in ROIs were converted to activities by multiplying with the calibration factor. Absorbed doses in the target region were calculated according to the methodology outlined in MIRD Handbook No. 20, using OLINDA/EXM software (version 1.1) (10).

$$S = e^{-\alpha D - \beta D^2} \quad \text{...(3)}$$

Biological Effective Dose (BED): In accordance with the linear-quadratic (LQ) model, the effect of radiation (E) is expressed as the logarithm of the survival fraction (S). D represents the absorbed dose (10)

$$E = -\ln(S) = \alpha D + \beta D^2 \quad \text{...(4)}$$

The effect is linearly related to the absorbed dose, and thus, the effect (E) in the LQ model is defined as BED.

$$BED = \sum_i D_i + \frac{\beta}{\alpha} \frac{t_{1/2}^{rep}}{t_{1/2}^{rep} + t_{1/2}^{eff}} \sum_i D_i^2 \quad \text{...(5)}$$

Statistical Analysis

The Mann-Whitney U test was utilized for data evaluation, with a significance level of $P<0.05$ considered statistically significant for the relationship between kidney absorbed doses and BED.

RESULTS

In this study, dosimetry of ^{177}Lu DOTATATE was performed on a total of 22 patients diagnosed with neuroendocrine tumors. The primary tumor origin in 64% of the patients was identified in the small intestine, 14% in the pancreas, 3% in the lungs, 4% in the colorectal region, and the origin could not be determined in the remaining cases. Ki indices ranged from 3% to 18% in two-thirds of the patients based on pathology results. The follow-up period for the patients undergoing dosimetry was 16-32 weeks (mean 24.04±3.53), and treatments consisted of 3-7 cycles (mean 5±1). GFR values were measured after the patients' most recent treatment cycle. Due to the substantial tumor uptake of ^{177}Lu DOTATATE, whole-body doses were found to be low. Kidney absorbed doses were in the range of 21-29 Gy (mean 24.32±3.5) on average, given the renal pathway as the predominant excretion route for the radiopharmaceutical (Table I).

Table I. Kidney absorbed and BED doses, GFR values of patients followed in treatment

Patient no	Cure number	Total renal dose (Gy)	Total renal BED dose (Gy)	Whole Body dose (Gy)	GFR (ml/min.)	Follow-up period (week)
1	6	21	23	1.6	92	26
2	5	21	23	NA	91	21
3	4	22	24	1,8	88	19
4	5	23	24	1,9	85	18
5	4	22	24	1,8	68	18
6	3	21	24	1,3	85	19
7	5	22	24	1,8	74	17
8	5	23	25	2,1	83	21
9	6	24	26	1,8	68	32
10	6	25	27	2,3	66	29
11	3	24	28	2,1	60	27
12	5	25	28	1,8	71	16
13	4	26	29	1,6	68	32
14	7	27	30	1,9	53	25
15	5	26	30	1,2	59	24
16	4	26	30	1,6	62	31
17	5	29	32	0,9	43	28
18	6	26	33	2,1	65	28
19	5	25	36	2,6	63	18
20	6	24	34	1,8	74	25
21	5	26	29	2,4	63	26
22	6	27	31	2,2	58	29
Mean±SD	5±1	24.32±3.5	27.9± 2.5	1.83±0.4	69.95±12.2	24.04±3.53

BED: Biological effective dose

Metastatic neuroendocrine tumor-diagnosed patients were administered ^{177}Lu DOTATATE after ^{68}Ga DOTATATE PET/CT imaging. Images obtained from ^{68}Ga DOTATATE and after 4 cycles of treatment for a 67-year-old male patient are depicted in Figure 1.

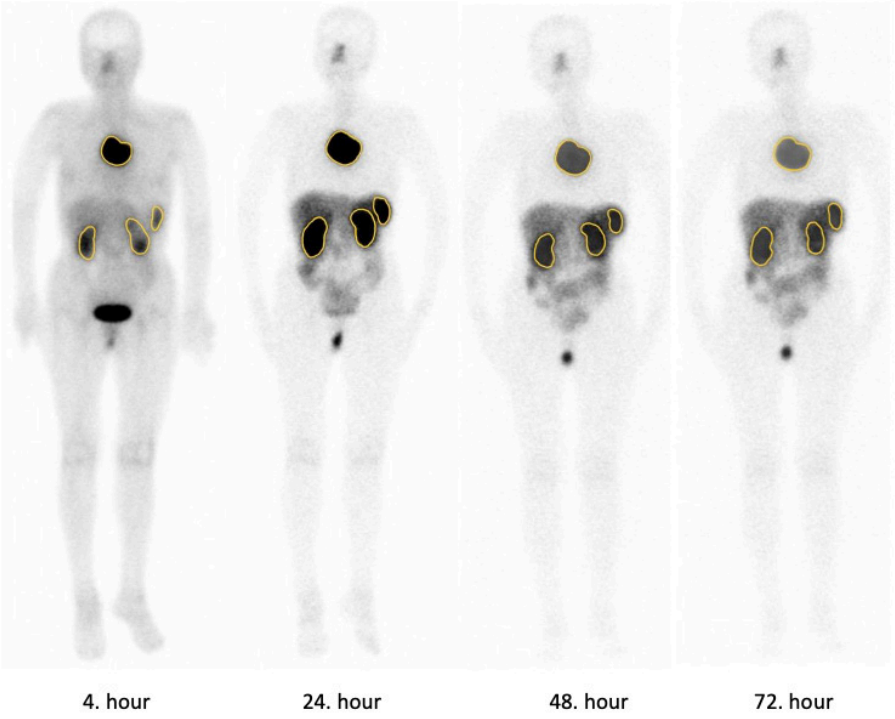
4. hour 24. hour 48. hour 72. hour

Figure 1. Whole-body scintigraphy images of the patient acquired at 4, 24, 48, and 72 hours for dosimetry of the neuroendocrine tumor using 177Lu-DOTATATE. The patient has a large neuroendocrine tumor located in the mediastinal region. Regions of Interest (ROIs) drawn over the tumor where the radiopharmaceutical shows intense uptake as well as over both kidneys and the spleen, are visible.

When total absorbed kidney doses were examined together with BED, it was observed that BEDs were approximately 14% higher than kidney doses in all patients (tole- rance dose) (Figure 2).

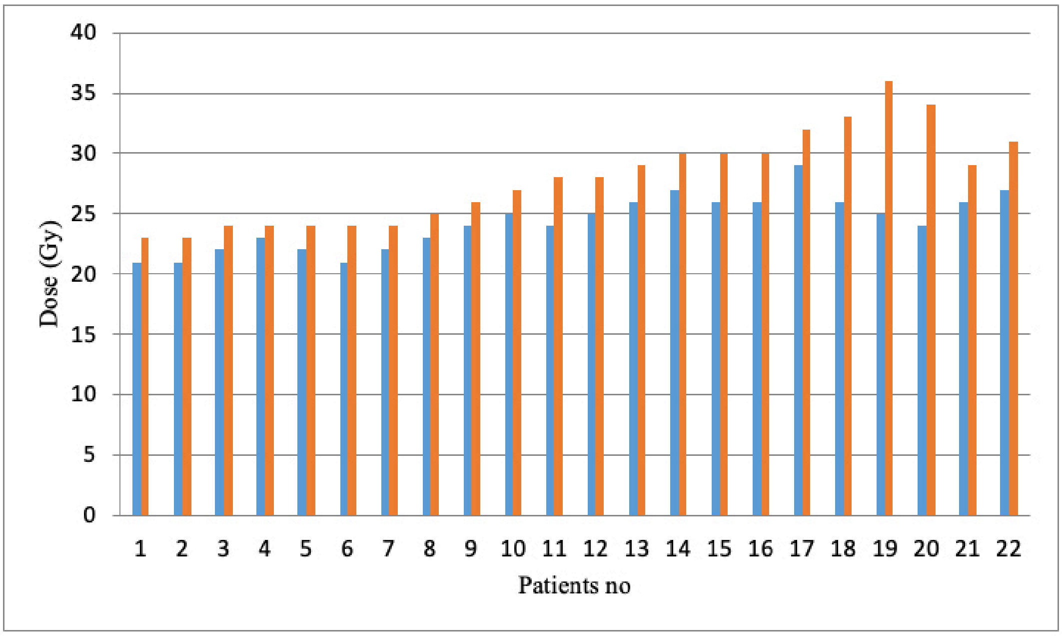

Figure 2. Comparison of absorbed kidney doses (in blue) with total biological equivalent doses (BED) (in red).

When BEDs were evaluated together with GFRs, it was determined that patients with lower BEDs had higher GFRs (Figure 3).

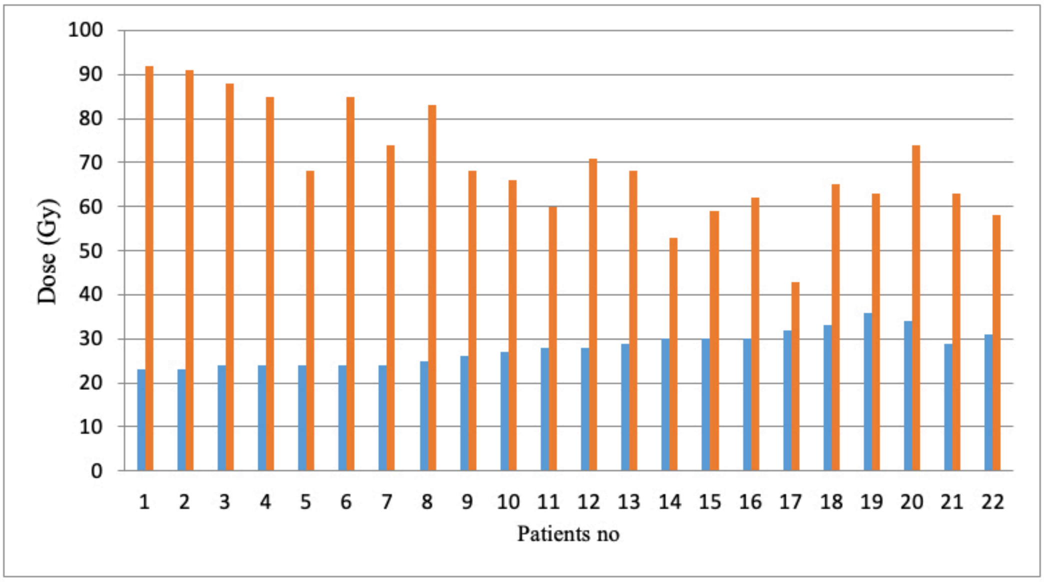

Figure 3. Comparison of total kidney BED dose (in blue) with kidney GFR values (in red).

When total kidney doses were evaluated together with GFRs, it was determined that patients with lower kidney doses had higher GFRs (Figure 4).

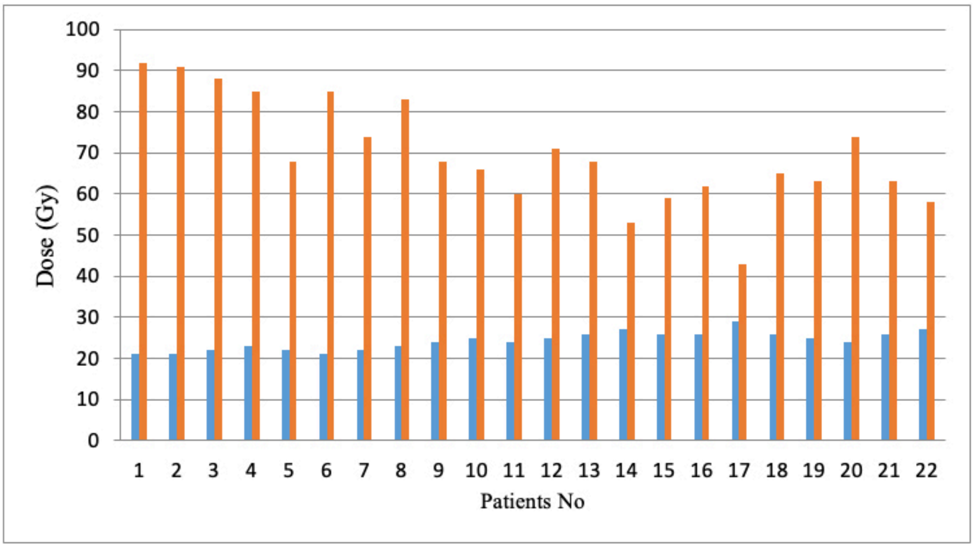

Figure 4. Comparison of kidney absorbed doses (in blue) with kidney GFR values (in red).

GFR >90 is considered normal, 60-89 is mild reduction, and 30-59 is moderate reduction. In our results, GFR was normal in 2 patients (9%), showed reduction in 4 patients (18%), and had a mild reduction in GFR in 16 patients (73%) (Figure 5).

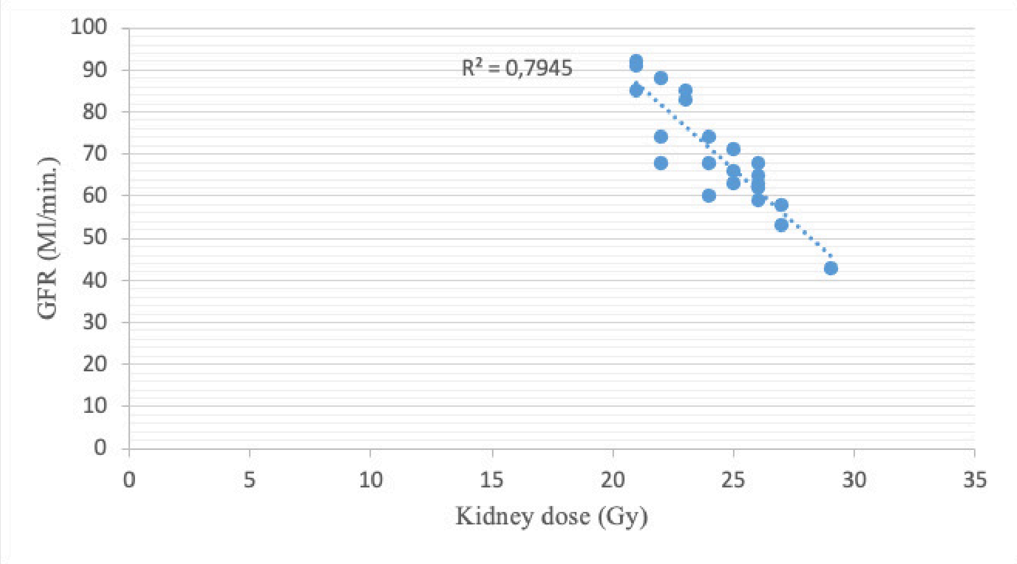

Figure 5. Correlation between kidney absorbed doses and GFR values.

Statistical evaluation

The significance between total kidney absorbed doses and total kidney BED doses was assessed using the Mann-Whitney U test, revealing a statistically significant difference at the p=0.0244 level.

DISCUSSION

In this study, dosimetry was performed on 22 patients receiving 3-7 cycles of ^{177}Lu-DOTATE treatment, and it was observed that as the absorbed kidney dose increased, the kidney BED value also increased. Additionally, patients with lower kidney GFR values were found to have higher absorbed kidney doses. Whole-body absorbed doses varied among patients, a phenomenon that could be attributed to differences in patients' biokinetics. The number of treatment cycles in our study did not show a significant relationship with GFR and kidney absorbed doses, whether in lower or higher ranges. Furthermore, a tolerance dose difference of approximately 14% was calculated between kidney BED and kidney absorbed dose (11).

Recent studies on ^{177}Lu-DOTATATE PRRT dosimetry have demonstrated that at least three imaging time points are required to accurately evaluate the biological phases. The most commonly used imaging times are at 4–6 hours on the day of radiopharmaceutical administration, day 2, and day 7 (12, 13). However, some studies suggest that imaging at 4 hours and day 2 is sufficient for the dosimetric calculation of radiopharmaceutical activity accumulated in the kidneys (14). Conversely, other researchers argue that this approach is not appropriate due to - variability in uptake (15). Therefore, for tumor imaging and obtaining reliable dosimetric data, at least two early and one late imaging time point are required.

On the other hand, some studies have reported that a single time point imaging at 24 hours is sufficient for ^{177}Lu-DOTATATE PRRT dosimetry. In particular, this single imaging time point has been considered reliable for estimating renal doses (16). The accuracy of single time point dosimetry also depends on the precision of the time-activity curve. The trapezoidal integration method, which relies on linear interpolation between data points, is the most commonly used approach for constructing time-activity curves. However, a significant limitation of this method is the estimation of the integrated area before the first imaging time point and after the last imaging time point (17).

Sandstrom and colleagues conducted studies on three-dimensional imaging-based clinical applications for solid organs in ^{177}Lu-DOTATE PRRT dosimetry (18). Ilan E. and colleagues emphasized the need for clinical studies on high dose limits for kidneys (19). In our study, we observed the importance of performing pre-treatment dosimetry for kidneys in terms of kidney toxicity. Sundlov A. and colleagues stated that the BED value of 38 Gy and the kidney absorbed dose limit of 23 Gy were effective in determining the number of cycles in multiple applied treatments (13). In our study, the BED value did not exceed 38 Gy in treatments ranging from 3 to 7 cycles.

Gustafsson J and colleagues, while expecting a longer retention time for 177Lu in normal tissues in patients with low GFR values, observed that this did not happen. They indicated that the reasons for this were related to the method used and tumor and physiological factors. In this study, it was determined that patients with high kidney absorbed doses had lower GFR values, and there was a good correlation between these two values. This authors reported that the kidney BED dose did not cause toxic effects up to 40 Gy and none of the patients included in this study exceeded a kidney BED value of 40 Gy (20, 21). Svensson and colleagues mentioned that in cases where kidney doses are high, lower GFR values are expected (4). In our study, we also observed lower GFR values when kidney dose values were high.

CONCLUSIONS

Renal toxicity is a significant factor in the treatment of neuroendocrine tumors with ^{177}Lu-DOTATE. In this study, although the total kidney dose and BED increased as the number of treatment cycles increased, rapid decreases in GFR were not observed, and none of the treated patients reached a toxic dose in their kidneys. It has been observed that performing dosimetry for each patient in the first treatment cycle is an important practice for evaluating renal toxicity and GFR in radionuclide treatments. Therefore, the importance of performing dosimetry in the treatment of neuroendocrine tumors with ^{177}Lu-DOTATE and determining specific dose limits for the patient has been emphasized through this study.

Limitations of this study

The study is recommended to be conducted on a larger number of patients to ensure statistical reliability.

Ethics Committee Approval

This research complies with all the relevant national regulations, institutional policies and is in accordance the tenets of the Helsinki Declaration, and has been approved by the Istanbul University Cerrahpaşa Medical Faculty Ethical Committee, (approval number: 83045809/604/5855).

Informed Consent

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions

Concept - A.A., N.Y.; M.D.; Design - A.A, N.Y; Supervision – A.A., M.D., N.Y.; Resources - A.A., N.Y.; Materials - A.A., N.Y.,; Data Collection and/or Processing - A.A., N.Y.; Analysis and/ or Interpretation - A.A., N.Y., M.D.; Literature Search - A.A., N.Y., Writing Manuscript - A.A., M.D.; Critical Review - A.A., N.Y., M.D.

Conflict of Interest

The authors have no conflict of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

REFERENCES

1. Kwekkeboom DJ, de Herder WW, van Eijck CH, Kam BL, van Essen M, Teunissen JJ. Eric P. Krenning , Peptide receptor radionuclide therapy in patients with gastroenteropancreatic neuroendocrine tumors. Semin Nucl Med 2010; 40:78–88.

2. Melis M, Krenning EP, Bernard BF, Barone R, Visser TJ, de Jong M. Localisation and mechanism of renal retention of radiolabelled somatostatin analogues. Eur J Nucl Med Mol Imaging 2005 ;32:1136– 43.

3. Erik S. Mittra Neuroendocrine Tumor Therapy:-177Lu-DOTATATE American Roentgen Ray Society 2018.

4. 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 ^{177}Lu-DOTATATE treatment. Eur. J. Nucl. Med. Mol. Imaging 2015; 42:947–55.

5. Sandström M, Garske-Román U, Johansson S, Granberg D, Sundin A, Freedman N. Kidney dosimetry during ^{177}Lu-DOTATATE therapy in patients with neuroendocrine tumors: aspects on calculation and tolerance. Acta Oncologica 2017; 57(4):516-21.

6. Gupta SK, Singla S, Bal C. Renal and hematological toxicity in patients of neuroendocrine tumors after peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE. Cancer Biother Radiopharm 2012; 27:593–9.

7. Siegel JA, Thomas SR, Stubbs JB, Stabin MG, Hays MT, Koral KF, Brill AB. MIRD pamphlet No. 16: techniques for quantitative radiopharmaceutical biodistribution data acquisition and analysis for use in human radiation dose estimates. Journal of Nuclear Medicine 1999; 40(2):37-61.

8. Wessels BW, Konijnenberg MW, Dale RG, Breitz HB, Cremonesi M, Meredith RF, Thomas SR. MIRD pamphlet No. 20: the effect of model assumptions on kidney dosimetry and response implications for radionuclide therapy. Journal of Nuclear Medicine 2008; 49(11):1884-9.

9. Stabin MG, Konijnenberg MW. Re-evaluation of absorbed fractions for photons and electrons in spheres of various sizes. Journal of nuclear medicine 2000; 41(1):149-60.

10. Sandström M, Freedman N, Fröss-Baron K, Kahn T, Sundin A. Kidney dosimetry in 777 patients during ^{177}Lu-DOTATATE therapy: aspects on extrapolations and measurement time points, EJNMMI Physics 2020; 7(1):73.

11. Sundlöv A, Sjögreen-Gleisner K, Svensson J, Ljungberg M, Olsson T, Bernhardt P, Tennvall J. Individualised ^{177}Lu-DOTATATE treatment of neuroendocrine tumours based on kidney dosimetry. European journal of nuclear medicine and molecular imaging 2017; 44:1480-9.

12. Delker A, Ilhan H, Zach C, Brosch J, Gildehaus FJ, Lehner S, Bartenstein P, Böning G. The influence of early measurements onto the estimated kidney dose in [(^{177})Lu][DOTA(0), Tyr(3)]Octreotate Peptide receptor radiotherapy of neuroendocrine tumors. Mol Imaging Biol 2015; 17(5):726–34.

13. King M, Farncombe T. An overview of attenuation and scatter correction of planar and SPECT data for dosimetry studies. Cancer Biother Radiopharm 2003; 18:181–90.

14. Knoll P, Rahmim A, Gültekin S, Šámal M, Ljungberg M, Mirzaei S. Szczupak B. Improved scatter correction with factor analysis for planar and SPECT imaging. Review of Scientific Instruments 2017; 88(9).

15. Ilan E, Sandström M, Wassberg C, Sundin A, Garske-Román U, Eriksson B, Lubbering M. Dose response of pancreatic neuroendocrine tumors treated with peptide receptor radionuclide therapy using ^{177}Lu-DOTATATE. J Nucl Med 2015; 56(2):177–82.

16. Hänscheid H, Lapa C, Buck AK, Lassmann M, Werner RA. Dose Mapping after endoradiotherapy with ^{177}Lu-DOTATATE/DOTATOC by a single measurement after 4 days. J Nucl Med 2018; 59(1):75–81.

17. Nautiyal A, Michopoulou S, Guy M. Dosimetry in Lu-^{177}-DOTATATE peptide receptor radionuclide therapy: a systematic review. Clinical and Translational Imaging 2024, 12(2): 157-75.

18. Sandström M, Ilan E, Karlberg A, Johansson S, Freedman N, Garske-Román U, Method dependence,observer variability and kidney volumes in radiation dosimetry of(177)Lu-DOTATATE therapy in patients with neuroendocrine tumours. EJNMMI Phys 2015; 2:24.

19. Ilan E, Sandstrom M, Wassberg C, Wassberg C, Sundin A, Garske–Román U, Eriksson B, Granberg D and Lubberink M. Dose response of pancreatic neuroendocrine tumors treated with peptide receptor radionuclide therapy using 177Lu-DOTATATE. J Nucl Med 2015; 56:177–82.

20. Garske U, Sandström M, Johansson S, Granberg D, Lundqvist H, Lubberink M, Eriksson B. Lessons on tumour response: Imaging during therapy with ^{177}Lu-DOTA-octreotate. A case report on a patient with a large volume of poorly differentiated neuroendocrine carcinoma. Theranostics 2012; 2(5):459.

21. Gustafsson J, Brolin G, Cox M, Ljungberg M, Johansson L & Gleisner KS Uncertainty propagation for SPECT/CT-based renal dosimetry in ^{177}Lu peptide receptor radionuclide therapy. Physics in Medicine & Biology 2015; 60(21): 8329.