Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Management of radioiodine ablation therapy in haemodialysis patients with thyroid cancer: a case series of two patients

Raymond Lin

raymond.lin@health.nsw.gov.au

Nepean Hospital

Alessandra Malaroda

Nepean Hospital

William J Ryder

Nepean Hospital

Veronica CK Wong

Nepean Hospital

Nikki L Wong

Nepean Hospital

Research Article

Keywords: Haemodialysis, radioiodine therapy, end-stage kidney disease, thyroid cancer, nuclear medicine

Posted Date: April 5th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4161082/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Radioiodine (^{131}I) therapy in treatment of thyroid cancer, has a biological clearance that is significantly reduced in end-stage kidney disease (ESKD), leading to increased radiation exposure and potential myelotoxicity. For ESKD patients on haemodialysis (HD), there is no standardized approach to ^{131}I administration and scheduling of HD following.

Methods

Two patients with ESKD on HD were treated with ^{131}I therapy for thyroid cancer. Local ^{131}I treatment protocol was modified to account for ESKD and HD. Modifications were made to existing infrastructure and additional patient and staff safety precautions were undertaken, including serum ^{131}I measurements to monitor for myelotoxicity.

Results

HD at 24-,72- and 144-hours post-^{131}I results in a retained radiation activity profile comparable to patients with normal renal function. Radiation dose to bone marrow throughout treatment was assessed at < 0.3 Gy for both patients. The highest contribution of radiation dose to bone marrow (60% and 47% for patient 1 and patient 2 respectively) was due to the radioactivity retained in blood before the first HD session. Cumulative radiation exposure to dialysis staff during therapy was well within local safety constraints. At 18 months post-therapy, remnant thyroid ablation was successful in both patients.

Conclusions

^{131}I therapy can be safely administered in patients with ESKD on HD with modifications to existing infrastructure and protocols. Serum ^{131}I measurements is a simple and minimally invasive method to assess bone marrow safety during treatment. Ongoing pooling of experiences is needed to inform a standardized protocol for therapy in this population.

Background

Ablative radioiodine (^{131}I) therapy with ^{131}I-sodium iodide following thyroidectomy is often prescribed as standard of care for patients with differentiated thyroid cancer (DTC). As radioactive ^{131}I is cleared primarily via the kidneys, prolonged blood retention of ^{131}I in patients with end-stage kidney disease (ESKD) requiring haemodialysis (HD) can result in an increased risk of myelotoxicity(1). For these patients, timing of HD sessions is critical since the extraction efficiency of hemodialysis of the

radioactive ^{131}I is greater than that of normal kidney function and, if not scheduled appropriately, can compromise the efficacy of the treatment. Moreover, in the days immediately after ^{131}I administration, these patients pose a radiation risk to nursing staff during HD, being themselves a source of g-radiation and from the radioactivity still retained in blood. Radioiodine treatment in HD patients thus presents logistical and clinical challenges for patients and clinical staff.

There is limited published guidance in the setup of the treatment protocol for radioablation of thyroid remnants in ESKD patients(2, 3) and literature is mainly limited to case reports and case series that feature a wide range of protocols and approaches(4). The paucity of literature in treating these patients contributes to the lack of consensus in the optimal treatment schedule to ensure treatment efficacy while limiting risks of myelotoxicity(5). With the objective of contributing our experience to the existing literature and the goal that pooled data from studies may build toward the development of a standardized treatment protocol for this patient population, we report a case series of two HD patients who underwent ^{131}I therapy in a tertiary centre in Sydney, Australia. The modified protocol for ^{131}I therapy in HD patients is described, with a report on the outcomes of treatment, and staff and patient safety measures, including whole-body and serum ^{131}I measurements as the additional safety monitor for myelotoxicity.

Methods

Population

Two HD patients with DTC received post-thyroidectomy adjuvant ^{131}I therapy. The comparator population was 10 consecutive patients with normal renal function that underwent ^{131}I therapy for thyroid cancer in the same year at the same centre.

Pre-Treatment Preparation

Several aspects of HD and ^{131}I therapy were considered, with modifications made to existing hospital protocols and infrastructure.

Room Preparation

Specific modifications were made to our hospital’s existing lead-lined room for radioiodine treatment. Plumbing to create a water supply and safe drainage for HD was installed under the supervision of the Radiation Safety Officer. A portable reverse osmosis machine (Baxter/Gambro WRO 300H) for water purification and HD machine (Fresenius Medical Care 5008S) was sourced. An important consideration is the isolation period required for both units after treatment completion; contaminated equipment is typically stored for ten half-lives (approx. three months for ^{131}I). There was existing closed circuit television (CCTV) monitoring in the room. The treatment room set-up is shown in Fig. 1.

Staff Safety and Education

The following additional precautions were instituted to optimise staff safety:

1. Radiation safety education sessions for all staff involved were conducted by the hospital Medical Imaging Physics Service.
2. Disposable personal protective equipment (PPE) was worn at all times within the room (face-shield, mask, gown, double-layered gloves and shoe covers) to protect against splash contamination.
3. HD nursing staff were given electronic personal dosimeters worn underneath PPE to monitor cumulative radiation dose during each HD session.
4. A physicist was available during all HD sessions to monitor staff radiation exposure and intervene in case of radioactive spill/contamination.
5. An area immediately in front of the lead door to the radioiodine room was covered with absorbent paper (Whatman® Benchkote) to allow for assessment of contamination of staff when exiting the room.
6. To minimize staff contact with the patients, patients were assessed for eligibility for self-cannulation and pre-trained if they were suitable.

Handling of HD consumables

All HD consumables in the ^{131}I treatment room were prepared and stored in the room before admission of the patient, limiting the time spent by nursing staff in the room during the HD sessions. Following HD, all consumables were disposed in a sharps bin labelled as mixed radioactive-biological waste. The waste was stored for ten half-lives (three months) and disposed as biological waste.

Handling of pathology specimens

For blood samples (serum biochemistry, full blood counts, coagulation studies) taken during HD, additional provisions were made for handling, isolation, and appropriate disposal in consultation with pathology laboratory staff. Radioactive samples were labelled and safely transported to the laboratory and were processed separately to avoid impacting the results of non-radioactive samples. Once processed, blood samples were collected by Nuclear Medicine staff and disposed appropriately.

Other waste

Any biological waste, including colostomy bags, were collected in bins labelled as mixed radioactive-biological waste and safely stored for ten half-lives of ^{131}I (three months). At the end of the storage period, radiation level in the waste was re-assessed and, if decayed below New South Wales (NSW) regulatory limits, disposed as biological waste. Non-biological waste was stored in double-layered bags and disposed of as general waste.

Treatment Protocol

Pre-treatment

24-hour urine creatinine clearance was measured one week before treatment to determine residual renal function. Pre-treatment with thyrotropin alfa (Sanofi Genzyme – Thyrogen®) to stimulate remaining thyroid cancer cells was given 48-hours before treatment. Thyrogen® dose was reduced to a single intramuscular dose of 0.9mg to account for significantly slower elimination in patients with ESKD(6). Routine HD was performed 24-hours before ^{131}I therapy. Patients' usual medications were continued but phosphate binders were withheld for the second patient due to potential binding effect observed with the first patient.

Treatment

Administered activity of 1GBq was decided based on the American Thyroid Association risk stratification which placed both patients in a low to intermediate risk for recurrence of malignancy. The aim of ^{131}I therapy was remnant thyroid ablation for both patients.

^{131}I-sodium iodide was administered orally on Day 0. A nuclear medicine whole body scan was acquired at 4- and 24-hours post-administration and dose-rates at 1m were measured at 1- and 4-hours post-administration. Patients with residual renal function were instructed not to void urine before the dose-rate measurement at 4-hours to allow determination of the calibration factor between administered activity and dose-rate measurement. Routine HD was performed on Days 1, 3 and 6, corresponding to 24-, 72- and 144-hours after ^{131}I administration.

Dose rates at 1m were taken on Days 1, 2, 3 and 6 post-^{131}I administration (on HD days (1, 3 and 6), the dose-rates were taken both pre- and post-HD). Patients were assessed for potential discharge from Day 3 by the hospital Medical Imaging Physics Service in compliance with state radiation safety legislation (*Radiation Control Act 1990 (NSW), Radiation Control Regulation 2013 (NSW)*). Dose-rate measurements were not scheduled on Days 4 and 5 (Saturday and Sunday) due to resource constraints. If the patient was not discharged on Day 3, they remained in hospital until Day 6.

Blood samples for bone marrow dosimetry were collected on HD days (Days 1, 3 and 6) pre- and post-HD. A standard of care nuclear medicine whole body scan was acquired on Day 3.

The timeline for the seven-day course of treatment is shown in Fig. 2.

Assessment of radiation dose to bone marrow

Approval from the Nepean Blue Mountains Local Health District Human Research Ethics Committee was sought for the collection of data for the assessment of radiation dose to bone marrow. Following the European Association of Nuclear Medicine (EANM) guidance(7), radiation dose to blood was assessed as an upper limit to the radiation dose to bone marrow.

Results

The baseline characteristics, including cancer staging and HD prescriptions, of the two study patients are shown in Table 1. Patient 1 was anephric due to bilateral nephrectomy and was undergoing ^{131}I therapy as a prerequisite for kidney transplantation listing. Patient 2 was morbidly obese (Body Mass Index 50) and had a colostomy in situ. Patient 1 was taught to and successfully self-cannulated for all HD sessions.

Table 1
Baseline characteristics, cancer characteristics and haemodialysis prescriptions of two haemodialysis patients undergoing radioiodine therapy. (*AVF = arteriovenous fistula, AJCC = American Joint Committee on Cancer*)

	Patient 1	**Patient 2**
Age (*years*)	41	60
Gender	Male	Male
Dry weight (*Kg*)	98	163
Estimated blood volume (*L*)	5.8	7.1
Urine output (*mL/day*)	0	630
24hr urine creatinine clearance (*mL/min*)	0	6
Dialysis duration (*hours*)	5	4.5
Dialysis membrane size (m^2)	2.5 (Solacea 21H)	2.1 (FX CorDiax 120)
Blood flow speed (*mL/min*)	300	300
Vascular access type	Radiocephalic AVF	Radiocephalic AVF
Thyroid cancer type	Papillary	Papillary
Lymph node involvement	Yes	Undefined
Stage (*AJCC 8th Edition TNM*)	I (T1b, N1, M0)	II (T2, NX, M0)
Notable considerations	Anephric	Morbid obesity
	Transplant candidate	Stoma

Initial nuclear medicine whole body scan at 4-hours post-^{131}I administration for patient 1 appeared to demonstrate pooling of radioactive material in the stomach, later dispersing on scans at 20- and 27-hours. This was postulated to be secondary to the presence of phosphate binders which were subsequently withheld for patient 2. Nuclear medicine whole body scan at Day 3 post-^{131}I therapy showed iodine-avid activity in the thyroid bed of both patients, with no activity seen elsewhere.

Retained radioactivity (%) as estimated from dose-rate meter measurements at 1m distance over Day 0 to 6 is shown in Fig. 3. The first sessions of HD resulted in a reduction in radioactivity of 76% and 67% in

Patient 1 and 2 respectively. Interdialytic reduction in radioactivity (between HD sessions 1 and 2) was low at 5.2% and 4.7% for patient 1 and 2 respectively.

Radiation Dosimetry

Total radiation dose to blood was estimated to be < 0.3Gy for both patients, much lower than the accepted maximum tolerated dose to blood of 2.0Gy(8). 60% and 47% of the radiation dose to blood was delivered in the time between ^{131}I administration and the first HD session, for patient 1 and patient 2 respectively.

Treatment Outcomes

Remnant thyroid ablation was successful in both patients. Patient 1 demonstrated a sustained reduction in thyroglobulin antibody titre and no evidence of structural disease recurrence. Patient 2 demonstrated sustained undetectable thyroglobulin. Thyroglobulin antibody levels pre- and post-treatment for patient 1 is shown in Fig. 4.

Exposure of Nursing Staff

No radioactive contamination was detectable on the nursing staff PPE. Nursing staff exposure to radiation based on personal dosimeter readings is shown in Fig. 5. Cumulative nursing radiation exposure across 3 sessions of HD was 7μSv and 23μSv for patient 1 and 2 respectively, well within the local dose constraint of 0.5mSv per year for the general public. Actual radiation exposure to individual nurses was even lower as dialysis nurses were rotated at each session. Cumulative radiation exposure for nursing staff assigned to patient 1 was notably lower than staff assigned to patient 2.

Equipment and radioactive waste

No radioactive contamination was detected on the HD machine, which was safe to be returned to the ward. For each patient, a 12L sharps bin containing HD machine disposables and needles used during dialysis sessions was stored as mixed biological-radioactive waste. A 5L biological waste bin was stored containing stoma bags for patient 2.

Discussion

In the treatment of DTC in ESKD patients requiring HD, the timing of the first HD session after ^{131}I administration and, to a lesser extent, the interval between subsequent sessions is critical in maximizing treatment efficacy and minimizing bone marrow toxicity. Previous studies have utilized a range of intervals to the first HD session, varying from 15-hours to 42-hours(4). The interval to subsequent HD sessions has also varied widely in these studies, ranging from 12-hours to 45-hours(4). The rationale behind the choice of HD scheduling in these treatments was dictated by differences in the administered activity of ^{131}I, readings of dose-rates from the patient, individual patient dialysis requirements, as well as resource availability.

The timing of the first HD session after administration is crucial as it determines the majority of radiation dose to the bone marrow. For instance, we found that 60% and 47% of the total radiation dose to bone marrow, for patient 1 and 2 respectively, was delivered in the time between ^{131}I administration and the first HD session. It follows that increases in the time between ^{131}I administration and the first HD session will significantly increase the radiation dose delivered to bone marrow. We estimated that the radiation dose delivered to blood was 0.15Gy and 0.1Gy for patients 1 and 2 respectively. If the first HD session were scheduled at 48-hours post-administration instead of 24-hours, we calculated that the radiation dose delivered to bone marrow increases to 0.3Gy and 0.2Gy for patients 1 and 2 respectively.

In our study, we found that performing HD sessions at 24-, 72- and 144-hours (Days 1,3 and 6) post-^{131}I produced a retained percentage radioactivity profile (i.e., overall clearance rate) similar to profiles of patients with normal renal function (Fig. 3). This HD regimen also mirrors the schedule for most patients who undergo 3 times/week intermittent HD, minimizing the risk of emergent dialysis (e.g., for fluid overload, hyperkalaemia) during radioablation treatment. As expected, clearance of ^{131}I between HD sessions was mainly due to the physical decay of the radionuclide. This is demonstrated through Patient 2, who had a creatinine clearance of 6mL/min, but did not show any greater clearance of radioactivity than Patient 1, who was anephric, indicating that the typical residual renal function of a chronic HD patient is not able to significantly contribute to inter-dialytic ^{131}I clearance. It should be noted that clearance of ^{131}I between dialysis depends on ^{131}I availability in blood and, to a lesser extent, on the amount of ^{131}I excreted via other means (such as sweat and saliva). The amount of ^{131}I circulating in blood relates to the volume of residual thyroid tissue after the surgery; patient 2 had greater ^{131}I uptake in the thyroid bed than patient 1 explaining the lower inter-dialysis clearance.

The dosage of ^{131}I is another uncertain factor, with conflicting evidence on whether to reduce, maintain or increase the standard dose of ^{131}I given the prolonged half-life and reduced clearance of ^{131}I in ESKD. Vermandel et al., in a case series of 6 patients, found a 30% reduction to standard ^{131}I dosing to achieve a balance of treatment efficacy with bone marrow toxicity(6). Holst et al., reached similar conclusions using mathematical modelling(9). Other studies, conversely, have recommended equivalent dosing or increased dosing of ^{131}I given higher clearance rates on HD and using individualized dosimetry to guide HD scheduling(10–12). Although our data is limited to only 2 patients, assuming that HD clearance of ^{131}I is independent of administered dose, it suggests that the administration of higher levels of radioactivity (up to 4GBq) could be safely given to ESKD patients when the first HD session is scheduled at 24-hours post-administration. Decisions on dosing in this population are beyond the scope of our paper but multidisciplinary input from nuclear medicine specialists, nuclear medicine physicists, endocrinologists and nephrologists is a requirement due to the role of HD in ^{131}I clearance and the influence on radiation dose to bone marrow.

Staff safety is another important consideration when administering ^{131}I. Patients with normal renal function undergoing ^{131}I radioablation treatment in hospital are usually isolated with minimal staff contact during their admission. However, patients requiring dialysis represent a deviation from routine

practice, as dialysis nursing staff are required to be in close proximity to patients during sessions, when the g-radiation from ^{131}I may pose a risk. These risks can be significantly mitigated with appropriate distancing, sensible positioning whilst preparing for HD and remote monitoring during HD. In our study, we achieved an overall cumulative radiation exposure to dialysis nursing staff that was very low, consistent with other studies(3). Furthermore, as the closest and most prolonged patient contact occurs during fistula cannulation, if the patient can be safely trained to self-cannulate, we showed that radiation exposure can be reduced even further, seen in the notably lower cumulative staff radiation exposure for patient 1 compared to patient 2 (Fig. 5).

Finally, our experiences with patient 1 during the study led to additional protocol modifications which were applied to patient 2. One such modification was the suspension of phosphate binders prior to treatment as we suspect this may have resulted in the aggregation of ^{131}I in the gastrointestinal tract seen on the 4-hour scan for patient 1. There is no literature studying the affinity of phosphate binders with ^{131}I, but given it is a non-critical medication, withholding all phosphate binders prior to therapy is a reasonable approach. We also found the reduction in thyrotropin alfa to a single dose from the standard of two, produced a more than sufficient response in TSH to proceed with treatment, in agreement with EANM guidance(6).

Conclusions

The use of radioiodine in patients with ESKD on HD presents logistical hurdles and additional considerations for patient and staff safety. Our study supports the consensus that radioiodine can be safely administered to patients on HD if performed with additional precautions.

The existing literature conveys a wide variation in protocols and there is not yet a standardization of approach to therapy in this population. Due to multiple patient variables and differences in resourcing across centers, it is not possible or practical to set out definitive parameters, but rather guidelines and practice points based on multi-center experiences will be invaluable for centers that encounter this scenario for the first time.

Our modified protocol outlines one approach to radioiodine in patients on chronic HD to add to published experience and contribute to the future development of standardized guidelines.

Abbreviations

CCTV Closed circuit television

DTC Differentiated thyroid cancer

EANM European Association of Nuclear Medicine

ESKD End-stage kidney disease

HD Haemodialysis

^{131}I Radioiodine therapy

NSW New South Wales

PPE Personal protective equipment

Declarations

Ethics approval and consent to participate

All experimental protocols in the study were approved by the Nepean Blue Mountains Local Health District (NBMLHD) Low and Negligible Risk Subcommittee and ratified by the NBMLHD Human Research Ethics Committee (HREC 2022/ETH01125). Informed consent was obtained from all participants in this study prior to collection of any samples or data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available due to protect patient privacy, but are available from the corresponding author on reasonable request.

Competing interests

Not applicable

Funding

Not applicable.

Author's contributions

R.L., A.M., W.J.R, V.C.K.W. and N.L.W contributed to conception and design of the study, drafting and editing of the manuscript, providing final approval of published version and agree to be accountable for all aspects of the work involved. A.M. and W.J.R. contributed to data acquisition, analysis and interpretation.

Acknowledgements

Not applicable.

References

1. Sisson JC, Freitas J, McDougall IR, Dauer LT, Hurley JR, Brierley JD, et al. Radiation safety in the treatment of patients with thyroid diseases by radioiodine 131I: practice recommendations of the American Thyroid Association. Thyroid. 2011;21(4):335–46.
2. Luster M, Clarke SE, Dietlein M, Lassmann M, Lind P, Oyen WJ, et al. Guidelines for radioiodine therapy of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging. 2008;35(10):1941–59.
3. Murcutt G, Edwards J, Boakye J, Davenport A. Hemodialysis of chronic kidney failure patients requiring ablative radioiodine therapy. Kidney Int. 2008;73(11):1316–9.
4. Kumar M, Subramanian K, Tanwar KS, Prabhahar A, Divyaveer S, Sood A, et al. Radioiodine Therapy in Patient with Differentiated Thyroid Cancer and End-Stage Renal Disease on Maintenance Hemodialysis: Case Report with Review of Literature. J Nucl Med Technol. 2022;50(3):228–32.
5. Ciarallo A, Rivera J. Radioactive Iodine Therapy in Differentiated Thyroid Cancer: 2020 Update. AJR Am J Roentgenol. 2020;215(2):285–91.
6. Vermandel M, Debruyne P, Beron A, Devos L, Talbot A, Legrand JF, et al. Management of Patients with Renal Failure Undergoing Dialysis During (131)I Therapy for Thyroid Cancer. J Nucl Med. 2020;61(8):1161–70.
7. Lassmann M, Hänscheid H, Chiesa C, Hindorf C, Flux G, Luster M. EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy. Eur J Nucl Med Mol Imaging. 2008;35(7):1405–12.
8. Benua RS, Cicale NR, Sonenberg M, Rawson RW. The relation of radioiodine dosimetry to results and complications in the treatment of metastatic thyroid cancer. Am J Roentgenol Radium Ther Nucl Med. 1962;87:171–82.
9. Holst JP, Burman KD, Atkins F, Umans JG, Jonklaas J. Radioiodine therapy for thyroid cancer and hyperthyroidism in patients with end-stage renal disease on hemodialysis. Thyroid. 2005;15(12):1321–31.
10. Morrish DW, Filipow LJ, McEwan AJ, Schmidt R, Murland KR, von Westarp C, Betcher KB. 131I treatment of thyroid papillary carcinoma in a patient with renal failure. Cancer. 1990;66(12):2509–13.
11. Magné N, Magné J, Bracco J, Bussière F. Disposition of radioiodine (131)I therapy for thyroid carcinoma in a patient with severely impaired renal function on chronic dialysis: a case report. Jpn J Clin Oncol. 2002;32(6):202–5.
12. Jiménez RG, Moreno AS, Gonzalez EN, Simón FJL, Rodriguez JR, Jimenez JC, et al. Iodine-131 treatment of thyroid papillary carcinoma in patients undergoing dialysis for chronic renal failure: a dosimetric method. Thyroid. 2001;11(11):1031–4.

Figures

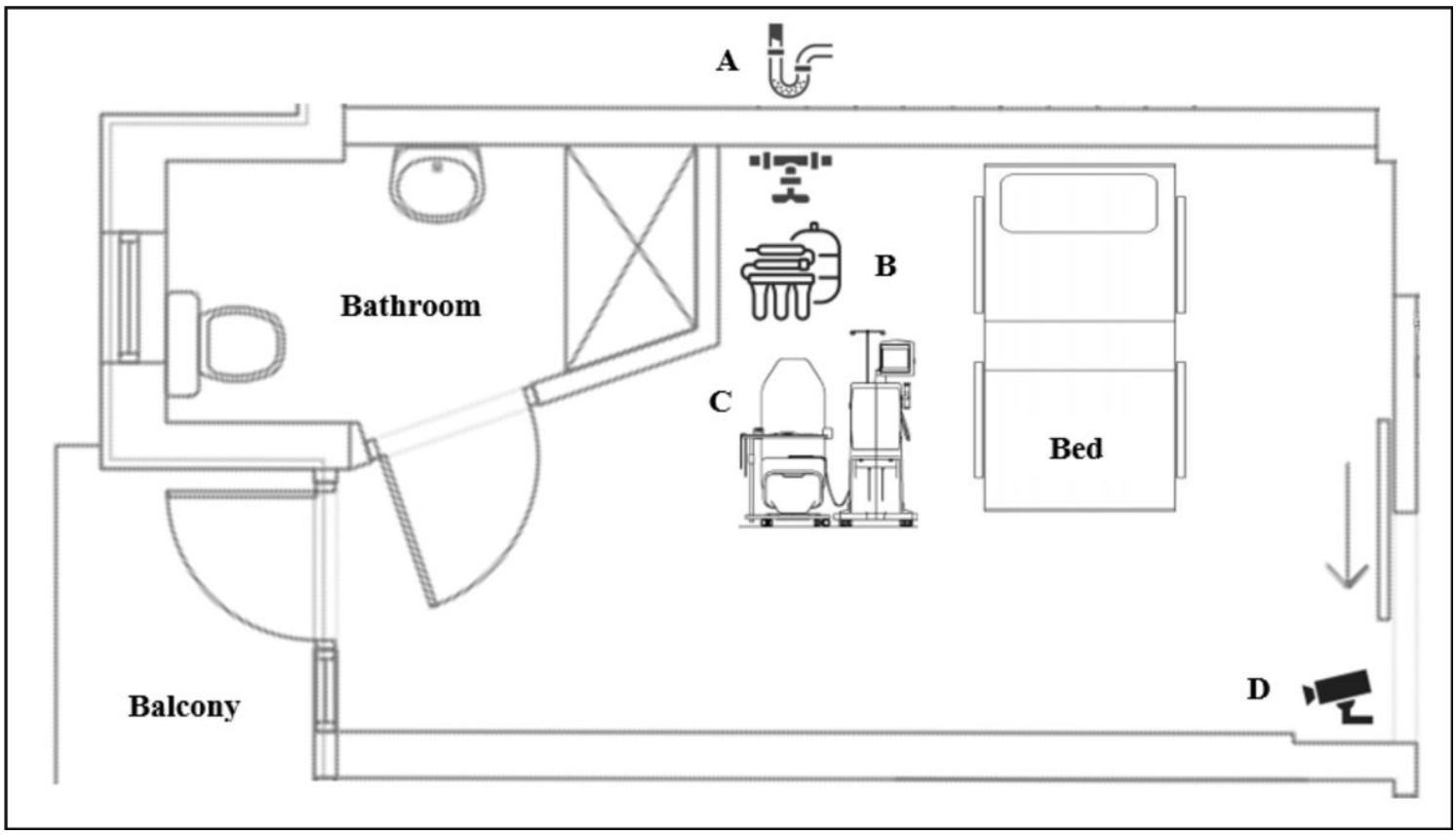

Figure 1

Floor plan of lead-lined treatment room. A – water supply and drainage unit. B – portable reverse osmosis machine. C – haemodialysis machine and chair. D – CCTV monitoring.

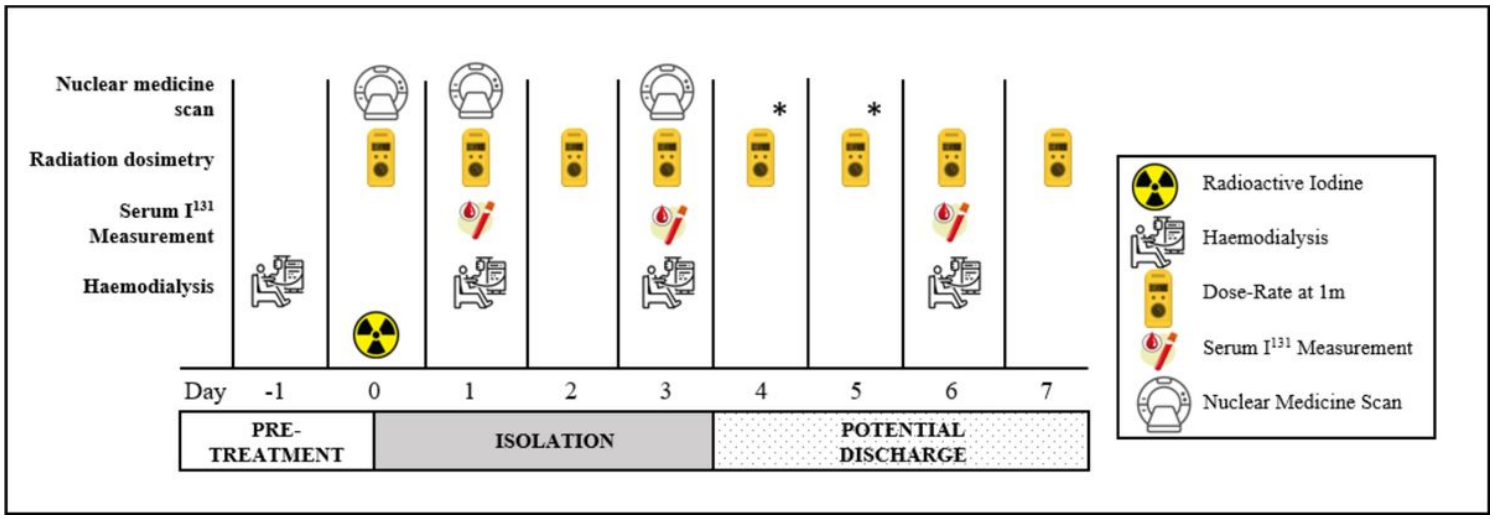

Figure 2

Radioiodine treatment timeline. Haemodialysis sessions were carried out on Day -1, 1, 3 and 6. Patients were assessed for potential discharge from Day 3. (*) Dose-rate measurements were not taken on Days 4

and 5 in our study due to resource constraints but should be taken if resources are available to aid earlier hospital discharge.

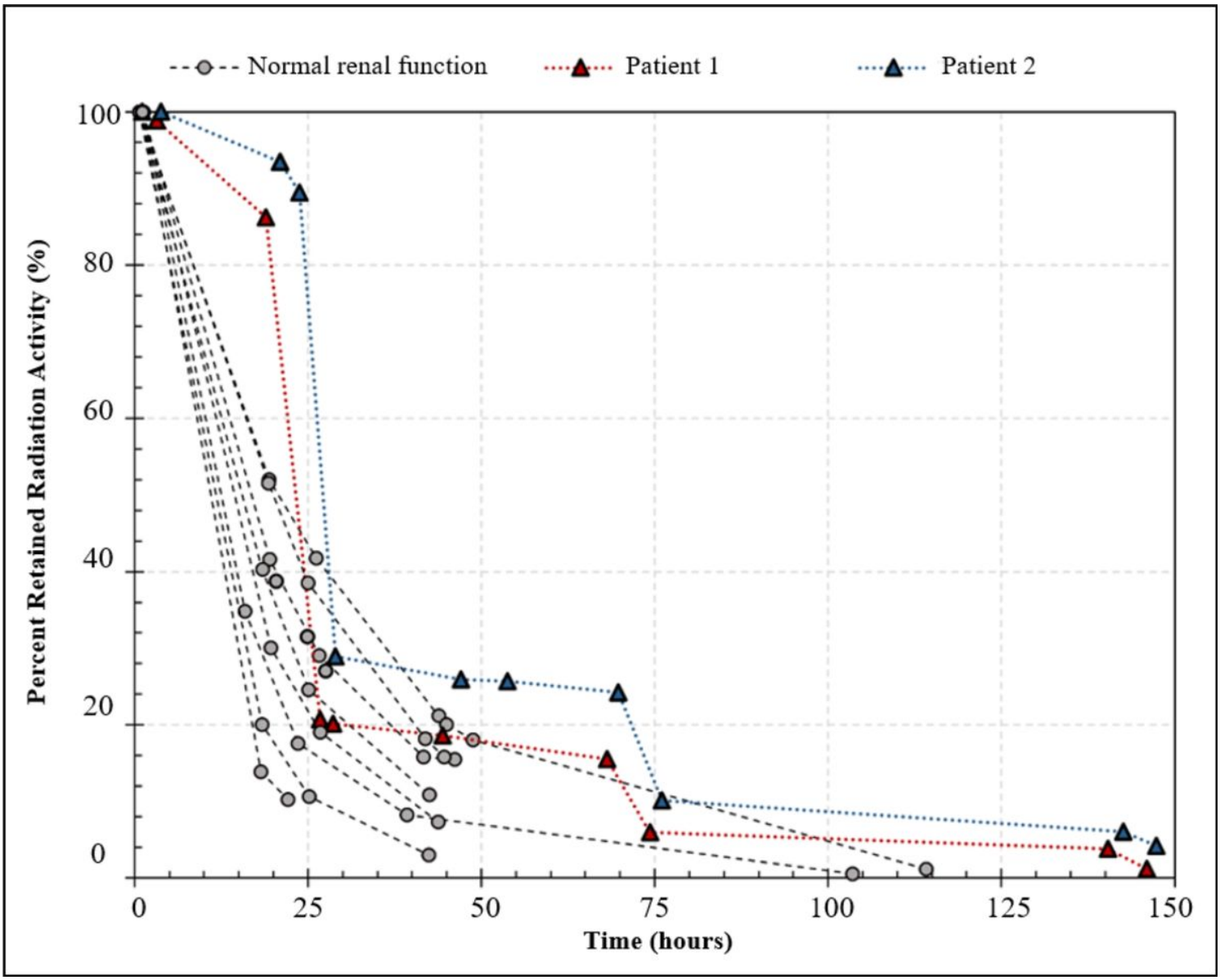

Figure 3

Retained radioactivity (%) over time. Haemodialysis sessions occurred at 24-, 72- and 144-hours post-^{131}I administration at 0-hours.

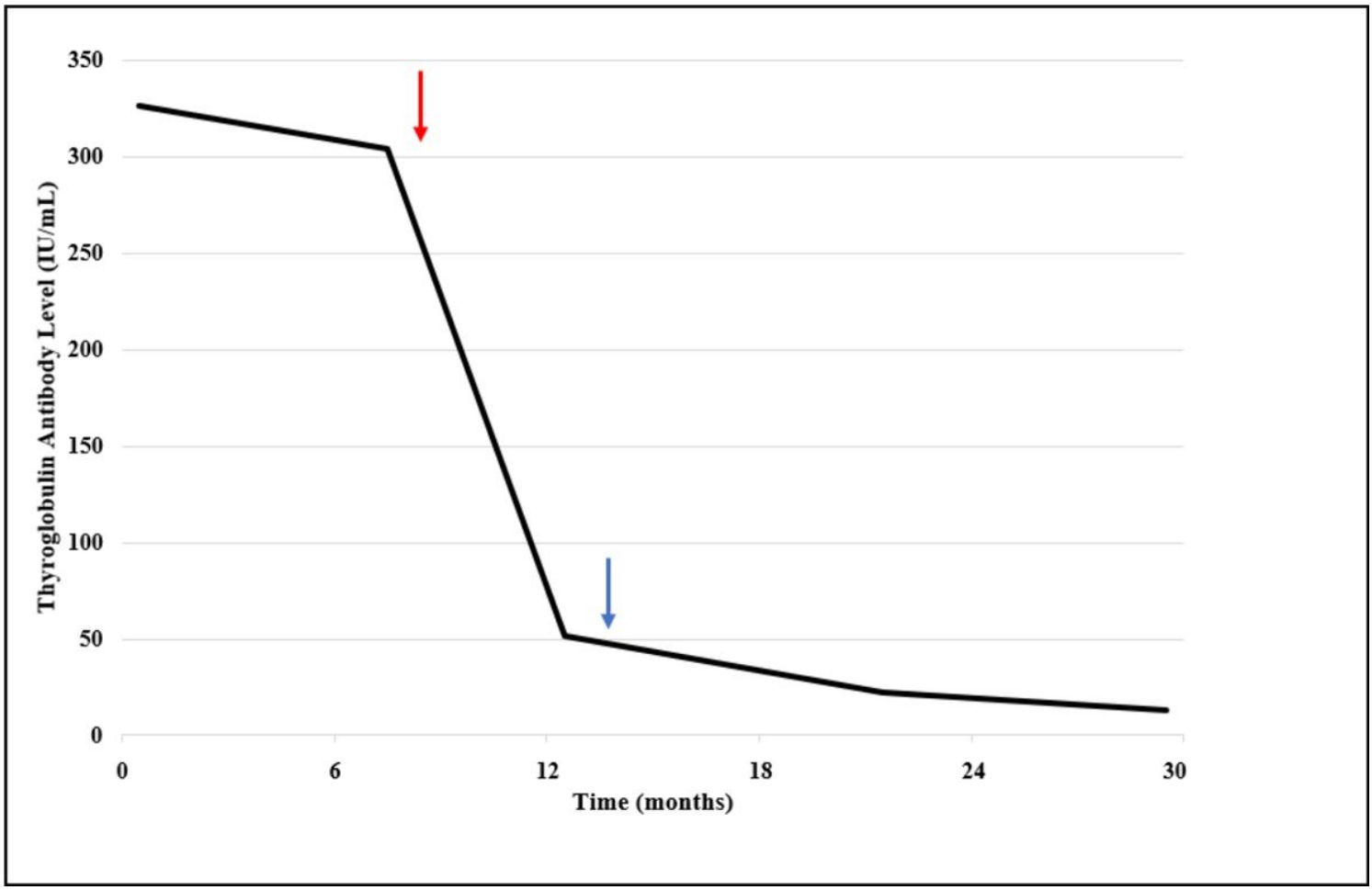

Figure 4

Thyroglobulin antibody levels for patient 1. Thyroidectomy is represented by the red arrow and ^{131}I therapy is represented by the blue arrow.

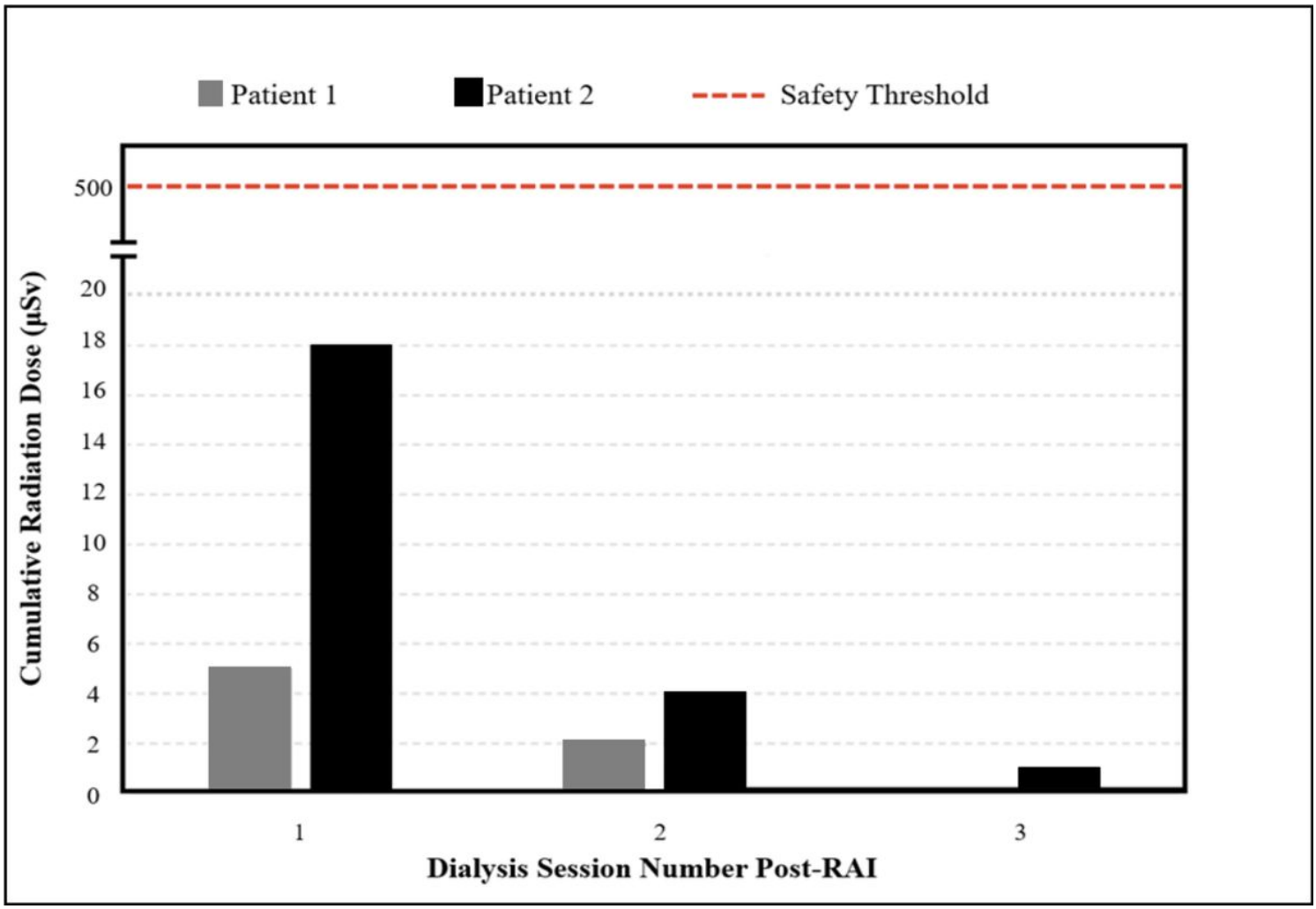

Figure 5

Cumulative radiation exposure to nursing staff across 3 haemodialysis sessions. Local constraints for safe radiation exposure threshold for the general public shown in red dotted line at 500µSv.