Delivery of Radioiodine Ablation in a Patient with End-Stage Renal Disease

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Abstract

Keywords

► thyroid carcinoma
► I-131
► hemodialysis
► end-stage renal disease

This case presents a pragmatic approach to the management of a radioiodine remnant ablation patient on hemodialysis which required no pretherapeutic dosimetric measurements. Pretreatment radiation dose modeling was performed using literature values for radioiodine hemodialysis extraction efficacies to determine a safe treatment regimen including adjustment of the administered activity and hemodialysis frequency. The pretreatment modeling was subsequently verified using external and blood radiation monitoring during treatment.

Introduction

Radioiodine remnant ablation (RRA) is considered to be a safe and effective method for eliminating residual thyroid tissue postthyroidectomy in patients with differentiated thyroid cancer. Radioiodine uptake by thyroid tissue is typically prompt with rapid renal clearance of excess radioiodine which minimizes radiation dose to healthy tissue. In patients with impaired renal function, careful consideration should be given to radioiodine administration to prevent radiotoxic effects.

Case Report

A 38-year-old lady with end-stage renal disease (ESRD) on home hemodialysis underwent subtotal parathyroidectomy for secondary hyperparathyroidism. Incidentally, the postoperative histology revealed two foci of classic variant papillary thyroid carcinoma (PTC) within 0.1 mm of the resection margin. There was associated lymphovascular invasion and one-third perithyroidal lymph nodes were also infiltrated with PTC. She then underwent completion left hemithyroidectomy, which yielded three further foci of PTC. Pathological staging was pT1b(m) pN1a Mx. Her pathology would be categorized as intermediate risk according to the American Thyroid Association. The role of postoperative radioiodine was considered taking into account the pathological factors and that the patient was a candidate for renal transplant.

If it were not for her impaired renal function, a radioiodine dose of 3.7 GBq (100 mCi) would have been considered. However, the administration of radioiodine poses a much higher risk to this patient due to the lack of renal function. Without renal clearance I-131 will remain in the body and irradiate healthy tissue. As such an appropriate hemodialysis regime and administered activity were chosen to keep the dose to healthy tissue in a safe range.

Literature indicates that dose to blood can be used as an effective surrogate for whole-body dose, which is much simpler to calculate.[1] The dose to blood is dependent on

the residence time of radioiodine in both the blood and whole body. This residence time is calculated as the infinite integral of fractional radioiodine retention with time or the area under the radioiodine retention curve (AUC). For prospective dose calculations, the whole-body residence time (T_{wb}) and blood residence time (T_{blood}) were assumed to be directly proportional. Therefore, a comparison of the area under the whole-body retention curves could be used as a coarse estimate of relative doses (i.e., $D_{blood} \propto AUC$). As such pretreatment dosimetry was performed comparing the AUC from proposed hemodialysis regimes against that from normal renal function measured in our population.[2]

Consideration was given to performing a more comprehensive pretherapy dosimetry regime (a low-dose administration with monitoring to determine retention characteristics) such as that recommended by the European Association of Nuclear Medicine (EANM), but this was considered impractical with additional concerns over thyroid stunning.[1]

Pretreatment modeling was performed using hemodialysis extraction efficacies from the available literature to model removal of radioiodine postadministration.[3] The patient is well established on a 48-hour hemodialysis regime at home ($\sim$ 75 L cleared over a 4-hour session). It was assumed for modeling that the patient had no residual renal function, consistent with clinical anuria (►Fig. 1).

When modeled, a 48-hour hemodialysis regime led to significantly increased whole body residence time (AUC) compared with typical renal function.

The optimal "dose" of hemodialysis remains uncertain. Traditionally anchored to a thrice-weekly regimen and typically expressed as a metric of small-solute (urea) clearance, hemodialysis dosing has been informed by numerous observational studies[4,5] and a few carefully conducted randomized clinical trials.[6] Solute removal can however be dramatically augmented by increasing the frequency of hemodialysis sessions.[7] Several uncontrolled studies showed that this approach can lead to significant improvements in patient-reported outcomes and laboratory results.[8] As such, most patients and their supervising clinicians take a pragmatic approach to long-term hemodialysis dosing; lifestyle

factors and vascular access burden are balanced against morbidity and mortality benefits of more frequent therapy. That said, in an acute setting (e.g., chronic hemodialysis patients requiring acute treatment), many components of the pre-existing hemodialysis prescription can be routinely altered; dialysis can be a flexible tool that can directly influence clinical care. Hence, a 24-hour hemodialysis regimen was proposed while the patient is in hospital (two sessions), returning to their typical 48-hour routine on discharge. This regimen results in a whole-body residence time approximately double that of a patient with typical renal clearance.

To account for this increase in retention, the administered dose was reduced by 40% from 3.7 GBq (100 mCi) to 2.2 GBq (60 mCi). As whole-body dose should be directly proportional to the administered activity, this dose reduction combined with the modeled hemodialysis regimen was expected to give a whole-body dose approximately 20% above that received by a typical patient. Using a typical value for patient whole-body dose of 0.65 Gy from a 3.7 GBq (100 mCi) I-131 treatment, the proposed regime has an anticipated whole-body dose of approximately 0.8Gy.[9]

The patient would dialyze in the morning of their treatment to allow 24-hour postadministration for uptake of the iodine by any thyroid remnant prior to removal by hemodialysis to maximize dose to target.

The pretherapeutic thyroid stimulation regime was also carefully considered given the absence of renal clearance. The standard Thyrogen regimen in patients with typical renal function is two intramuscular injections of 0.9 mg Thyrogen 24 and 48 hours before treatment. However, elimination of Thyrogen is significantly slower in dialysis-dependent patients with ESRD. As such a single dose of Thyrogen was given 48 hours prior to treatment based on clinical judgement in line with the literature (►Fig. 2).[3]

The patient was admitted to the radionuclide therapy suite consisting of a radiation-shielded side room with en-suite facilities in the hospital's oncology ward. Prior to treatment the room had been plumbed to allow a hospital hemodialysis system to be installed with direct discharge to
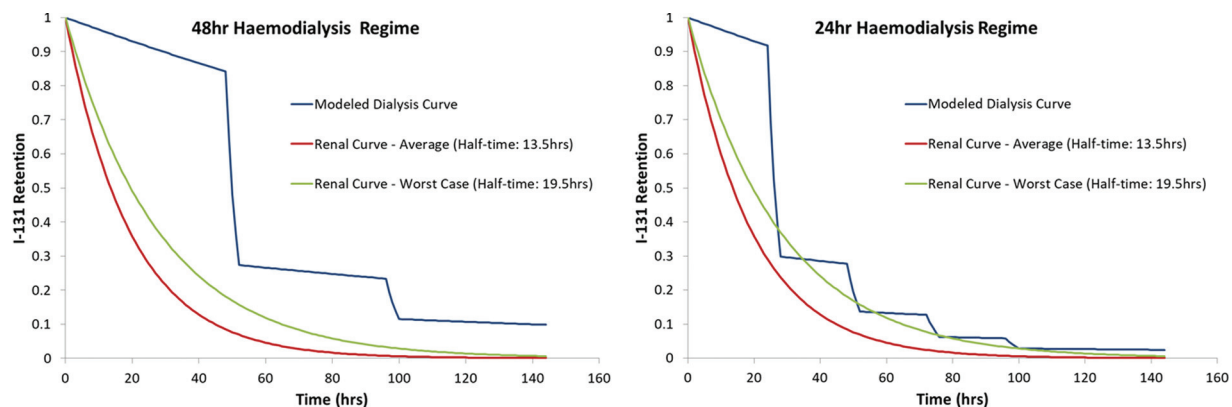

Fig. 1 Plot showing the radioiodine retention modeling performed pretreatment for 48-hour and 24-hour hemodialysis regimens. Retention curves for normal and worst-case renal function in the hospital population included.

Date	Treatment Interventions	Haemodialysis regime
Monday	0.9 mg Thyrogen injection in oncology out-patient clinic (afternoon post dialysis)	Dialyse (morning) at home <u>before</u> Thyrogen injection
Tuesday	No intervention	No dialysis
Wednesday Day of treatment	Admit to radioiodine suite on oncology ward (AM) Give I-131 treatment dose <u>after</u> dialysis	Dialyse on ward (AM) <u>before</u> giving radioiodine
Thursday	-	Dialyse (AM)
Friday Planned hospital discharge	*PM:* Planned discharge home after dialysis depending on safe radiation levels	Dialyse (AM)
Sunday	-	Dialyse at home and return to 48 hr dialysis regime.

Fig. 2 Planned treatment and hemodialysis schedule for the patient.

designated radioactive drains. The patient's pretreatment hemodialysis was performed using the in-room equipment to ensure the equipment functioned as expected.

Radioiodine administration was performed as standard via oral capsule.

To measure radioiodine retention, instantaneous dose rate measurements were performed before and after each hemodialysis session and at postablation imaging. In addition, blood samples were taken pre and post both hospital hemodialysis sessions (►Fig. 3).

Based on external dose rate measurements, the first hemodialysis session was less effective than expected at removing radioiodine (54% removal). The following sessions were in line with the extraction values found in the literature (47.5 ± 0.8)%. Both hospital hemodialysis sessions also started several hours earlier than planned based on dialysis

unit staff availability. Combining these effects led to an AUC approximately 2.1 times that of a patient with typical renal clearance.

Blood measurements show that the blood activity concentration follows a similar pattern to external dose rate but drops below the external dose rate retention value immediately after hemodialysis, re-normalizing to it before the next dialysis session.

The patient was discharged home after two nights of inpatient stay as planned. Radiation protection advice was given as standard with the time periods adjusted to account for the unique clearance characteristics.

Post discharge there was no detectable radiological contamination of the dialysis equipment after the consumables had been removed. As such the dialysis machine was returned to general use (►Fig. 4).
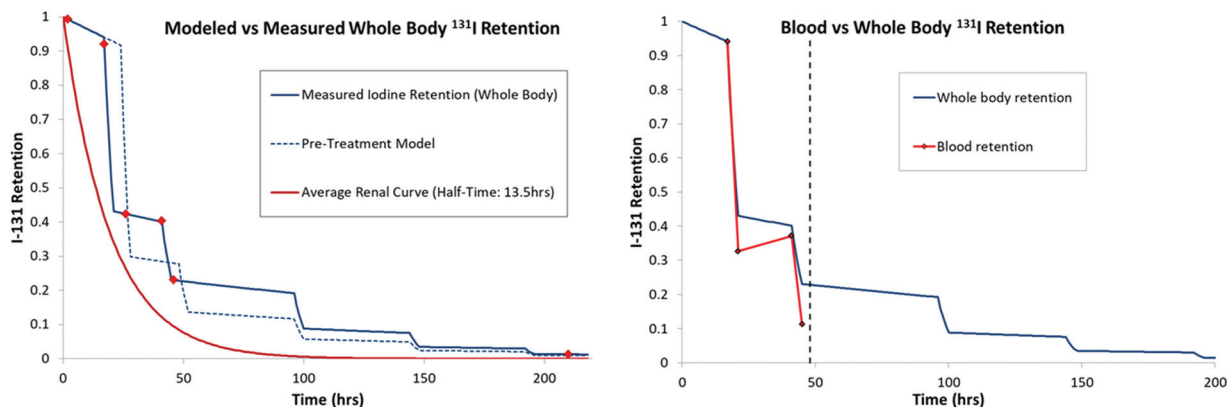

Fig. 3 Plots showing the radioiodine retention curves based on measurements performed during treatment against the pretreatment modeling.
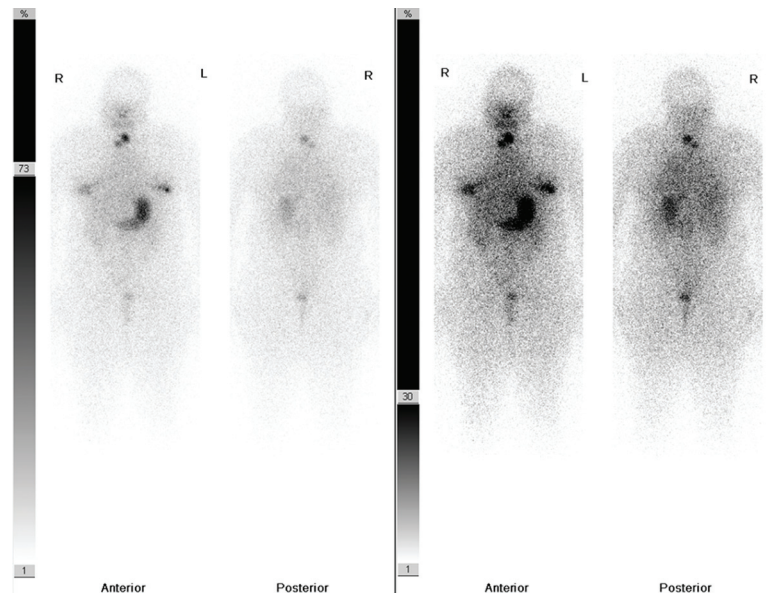
Fig. 4 Postablation images taken at +9 days from treatment showing uptake in the thyroid bed and elevated background and physiological uptake consistent with the increase in radioiodine retention.

The patient returned for a postablation scan at +9 days from treatment and a final external dose rate measurement. Imaging showed an elevated soft tissue background, in keeping with radioiodine retained in blood and extracellular water. The study was reported by a consultant radionuclide radiologist as showing focal uptake in thyroidectomy bed in keeping with remnant tissue. Further uptake in the breasts and stomach was reported as physiological.

Using MIRD (Medical Internal Radiation Dose) methodology and the measured iodine retention data, the whole-body radiation dose (estimated using dose to blood) is calculated as 0.97 Gy.[1,10] The patient reported no side effects consistent with radiotoxicity.

Discussion

This report presents a pragmatic approach to the management of a RRA patient on hemodialysis which required no pretherapeutic dosimetric measurements. As such a cautious approach was successfully applied to ensure a whole-body radiation dose was kept at tolerable levels.

The reduction in dose was driven by a desire to keep the whole-body radiation dose below any toxic effects and ideally comparable to the dose received by a patient with typical renal function. This target was achieved with a whole-body dose of below 1 Gy. This dose is well below the EANM-recommended limit of 2 Gy to blood but slightly above the typical dose to a radioiodine patient.[1]

The measured correlation of the blood and whole-body radioiodine retention supports the assumptions used in pretherapeutic modeling that the whole body and blood retention curves can be assumed to be directly proportional. This significantly simplifies pretherapeutic dosimetry in comparing proposed treatment regimes.

The brief reduction in blood activity below the whole-body retention curve following hemodialysis has not been reported in previous literature. This effect is likely redistribution of the radioiodine from the extracellular fluid back to blood post-hemodialysis. However, modeling this behavior in dose estimates is difficult as the equilibration time for radioiodine concentration between blood and extracellular water is unknown.

Several case studies have detailed RRA treatment in dialysis patients using 48-hour dialysis regimes.[3] However, in this case a 24-hour regime while being hospitalized allowed a much greater activity to be administered for the same whole-body dose, which should increase target dose and hence therapeutic effect.

There is no single metric to determine if RRA was successful and results of her dynamic risk stratification assessments are awaited. In this case post, treatment ablation scans showed uptake in the thyroid bed, indicating some therapeutic effect has been delivered and qualitatively the uptake in the thyroid remnant is comparable to that seen in postablation scans of patients with typical renal function.

Conflict of Interest
None.

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