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Management of patients with renal failure undergoing dialysis during 131I therapy for thyroid cancer

Dialysis During 131I Therapy

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Compliance with ethical standards

- **Conflict of interest**: None.
- **Research involving human participants**: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Keywords: thyroid cancer, radiotherapy, renal chronic failure, hemodialysis, toxicity, therapeutic efficacy, dosimetry, radiation protection.

Abstract

Objectives: Radioactive iodine (^{131}I) therapy may be used to treat thyroid cancer in end-stage renal disease patients who undergo hemodialysis. Because iodine predominantly utilizes renal clearance, treatment management in hemodialysis patients may be problematic, and no formal recommendations on hemodialysis currently exist. This work details our experience with treating thyroid cancer with iodine in chronic renal failure patients who require hemodialysis and details the therapeutic dosimetry results obtained during treatment to ensure that the dose to the bone marrow (BM) was acceptable.

Methods: We treated 6 patients in the metabolic radiotherapy unit after thyroid stimulation. Two hemodialysis sessions in the metabolic radiotherapy unit were performed at 42 and 90 hours after radiopharmaceutical administration. BM toxicity was estimated with activity measurements from blood samples and with whole-body measurements that were regularly repeated during hospitalization and measured with a gamma counter. The patients underwent thyroid and hematologic monitoring to assess treatment efficacy and therapeutic toxicity in the short, medium and long term.

Results: Whole-body activity was reduced on average by 66.7% [60.1-71.5] after the first dialysis session and by 53.3% [30.4-67.8] after the second. The mean estimated total absorbed dose to the BM was 0.992 Gy for all patients [0.431 – 2.323]. We did not observe any significant hematologic toxicity, and the clinical, biological and ultrasound test results confirmed the success of ablative treatment for the majority of patients.

Conclusion: An approximately 30% reduction from the nominal dose in the amount of ^{131}I activity for hemodialysis patients with thyroid cancer appears to strike an appropriate balance between the absence of BM toxicity and therapeutic efficacy. To avoid overirradiation, we recommend pretherapeutic dosimetry studies for metastatic patients to calculate the amount of activity to be

administered as well as dosimetry monitoring during the hemodialysis sessions performed after therapeutic dose administration and under the same conditions.

INTRODUCTION

The management of patients with thyroid cancer usually includes partial or total thyroidectomy with possible lymph node dissection followed by ^{131}I-ablative therapy for incomplete resection or intermediate-risk or high-risk tumor recurrence (*1*). Iodine-131 (^{131}I) radiotherapy is therefore recommended for most differentiated thyroid carcinoma patients after complete resection to destroy residues in the thyroid parenchyma (a priori benign), to facilitate follow-up care and to treat possible locoregional or distant tumor foci (metastases) (*2-4*). An extension assessment performed alongside ^{131}I radiotherapy by scintigraphy aims to adapt the management strategy, facilitate biological monitoring (thyroglobulin) and ultrasound imaging, and improve overall and progression-free survival for these patients (*5*).

^{131}I is a β- and γ-emitter with a radioactive half-life of 8.1 days. ^{131}I radiation is mainly composed of β- particles with a maximum energy of 606 keV, a mean energy of 192 keV and γ rays of 364 keV, allowing for both the treatment of patients and scintigraphic imaging (*6,7*). After oral administration of ^{131}I, only approximately 20% of the blood iodine is absorbed by the thyroid tissue; the remainder is largely cleared through the urine (up to 75%) (*8*).

The incidence of cancers, including thyroid cancer (*9,10*), is relatively higher in patients with chronic renal failure than in patients with healthy kidneys. Although several explanations have been proposed, the pathogenetic mechanism is still not fully understood (*11*).

Internal radiotherapy using high amounts of ^{131}I activity is difficult in these patients for the following reasons (*12,13*):

- increased irradiation of the patient (and to his or her close family and exposed caregivers) arising from the long biological residence period of the isotope due to limited or absent urinary excretion, which risks exceeding the limiting dose to the hematopoietic marrow and causing hematologic toxicities;

- the need for a practical facility for dialysis (in a radiation-protected unit or in a hemodialysis department) and adapted management strategies for the radioactive effluents produced during the first few dialysis sessions following iodine therapy.

The nuclear medicine department has dedicated facilities and procedures for monitoring and controlling the risk of exposure to ionizing radiation. However, hemodialysis patients require a controlled dialysis fluid elimination system as well as highly thorough radioactivity monitoring because the radiopharmaceuticals cannot be eliminated through the renal system. The realization of hemodialysis within the nuclear medicine department allows for optimal radiation protection conditions without the need for human intervention to discard the effluents, which can be directly evacuated to decay tanks. However, currently, very few centers meet the conditions needed to perform hemodialysis sessions from the nuclear medicine department.

Thus far, a limited number of studies have focused on the management of ^{131}I therapy in hemodialysis patients, and currently, no official hemodialysis recommendation exists (*14,15*).

This work reports our experience with managing ^{131}I treatment for thyroid cancer patients with chronic renal failure who are undergoing hemodialysis and the pretreatment dosimetry results obtained during their treatment.

MATERIALS AND METHODS

Patients

This retrospective study was conducted in the Nuclear Medicine Department of the Roger Salengro Hospital of Lille University Hospital and performed in accordance with the Declaration of Helsinki and national regulations. Since the procedures described were performed as the standard of care,

the institutional review board approved this retrospective study, and the requirement to obtain informed consent was waived.

From 2011 to 2017, we included hemodialysis patients with end-stage renal disease and thyroid cancer for whom systemic ^{131}I treatment was recommended following a multidisciplinary team meeting involving specialists in nuclear medicine, endocrinology and nephrology. The diagnosis of thyroid cancer was confirmed by an anatomopathological examination of the operative specimen after thyroidectomy. ^{131}I activity prescription was reduced from the nominal dose (i.e., 3700 MBq) and validated by the multidisciplinary team according to the risk of relapse. When considering a high risk of relapse, the activity ranged from 100% to 60% of the nominal dose (i.e., 2200 to 3700 MBq). When considering a low risk of relapse, the activity was reduced to 50% of the nominal dose (i.e., 1850 MBq).

A consultation prior to iodine therapy was systematically scheduled to examine the patient, confirm the absence of contraindications to the treatment, explain the course of hospitalization including the dosimetry study and explain the radiation protection instructions. In women of childbearing age, even though the risk of pregnancy was low, the absence of pregnancy and breastfeeding was verified, and the need for effective contraception for 6 to 12 months following treatment was explained.

Hospitalization

Optimal ^{131}I uptake to the thyroid parenchymal tissue (follicular cells) requires prior stimulation with thyroid stimulating hormone (TSH). This stimulation may be a thyroid hormone withdrawal (THW) for at least 4 weeks or intramuscular injections of recombinant human TSH (THYROGEN®: thyrotropin alfa, Genzyme, Cambridge, Massachusetts, USA).

The standard Thyrogen® regimen in patients with preserved renal function is two intramuscular injections (or subcutaneous injections if the patient is taking anticoagulants) of 0.9

mg Thyrogen® spaced 24 hours apart, with the first injection two days before and the second injection one day before ^{131}I treatment administration. In hemodialysis patients, a single injection of Thyrogen® was performed 48 hours before treatment to avoid an excessive TSH level and prolonged period of TSH elevation. The high TSH levels already observed in dialysis patients are associated with side effects such as headache or diarrhea.

The patients were hospitalized for five days to allow for dosimetry studies and dialysis in shielded rooms of the nuclear medicine department. Portable hemodialysis equipment was installed in the patient's room.

On the day of treatment, the patients underwent a dialysis session in the nephrology department before being transferred to the nuclear medicine department. After admission into the metabolic radiotherapy unit, an iodine capsule was orally administered to the patient by the referring physician (the administration was after urination in case of residual diuresis). The day and time of administration and the activity ingested were carefully noted. The capsule was systematically distanced from any factors that could influence the absorption of ^{131}I (particularly gastric protective treatments).

Iodine-131 whole-body scintigraphy was performed 3 days after treatment with a Siemens Symbia T series gamma camera (Siemens Healthcare, Erlangen, Germany) to conduct the locoregional extension assessment of the thyroid remnants and cervical ganglionic foci or distant foci (metastases).

When leaving the nuclear medicine department, the patients received radiation protection instructions again in a document that specified the dose rate at 1 meter measured on the day of discharge. The main instructions were to avoid prolonged contact with pregnant women and children under 10 years of age for the few days following the administration of ^{131}I and to reinforce their usual daily hygiene habits.

Prior to the hemodialysis sessions, regulatory controls of the water circuit were repeatedly carried out by the biomedical engineering department to ensure consistency. All of our patients had arteriovenous shunts so that they could benefit from regular hemodialysis sessions. Before being hospitalized in the nuclear medicine department, a hemodialysis session of 3 to 4 hours was conducted in the hemodialysis department of Lille University Hospital. Subsequently, the patients underwent two hemodialysis sessions using a transportable dialysis machine in the nuclear medicine department under the guidance of nurses trained in hemodialysis.

The dialysates were directly eliminated through connections to the decay tanks before being released into the public sewage treatment system (after approximately 4 to 5 months of decay). The disposable materials used during the hemodialysis sessions were managed as typical radioactive waste of the department. Radiation exposure to the staff was monitored using passive and operational dosimeters worn at chest level. Our radiation protection protocol for staff members is in accordance with the regulations issued by the French Nuclear Safety Authority. The radiation limit for nonoccupationally exposed personnel (e.g., dialysis nurse) and for the general public is 1 mSv/year, and the exposure limit for nuclear medicine staff is 6 mSv/year.

During hospitalization in the metabolic radiotherapy unit, blood tests for thyroglobulin (Tg), anti-thyroglobulin antibodies (anti-Tg Abs) and TSH were performed once or twice daily to study their respective kinetics directly after the administration of ^{131}I, particularly in the context of hemodialysis. In parallel, blood counts were performed before and after treatment to verify the absence of hematologic toxicity that may occur following the administration of ^{131}I.

Estimation of the BM absorbed dose

According to recommendations, the acceptable absorbed dose to the BM is limited to 2 Gy. The BM dose calculation is complex, but the dose to the blood, which is easier to determine, is an

accepted and satisfactory substitute (*16*). Thus, for the thyroid cancer treatments, given the different radioactive emissions of ^{131}I, the blood (target) is irradiated either by β-particles emitted by the activity of the blood itself (1st source) or by penetrating γ-radiation from the activity dispersed through the rest of the body (2nd source). Therefore, only blood and whole-body measurements should be monitored for radioactivity.

The method used in this study to calculate the absorbed dose to the BM is based on the medical internal radiation dose (MIRD) formalism (*17*), which was initially reported in the European Association of Nuclear Medicine (EANM) Dosimetry Committee series on "standard operating procedures" for BM dosimetry in the treatment of differentiated thyroid cancer (*16,18*). This method requires mathematical modeling and a direct measurement of the concentration of radionuclide activity as a function of time in the patient's body and enables dose calculation using eq. 1:

$$\overline{D_{blood}} = A_0 \times (S_{blood \leftarrow blood} \times \tau_{blood} + S_{blood \leftarrow body} \times \tau_{body}) \quad (1)$$

where

- $\overline{D_{blood}}$ [Gy] is the mean absorbed dose to the blood;
- A_0 [GBq] is the administered activity;
- $S_{blood \leftarrow blood}$ [Gy.ml.GBq^{-1}.h^{-1}] is the S value from the MIRD formalism and is used to estimate blood self-irradiation. Only β$^-$ contributions were considered, and the value from (*19*) was used: $S_{blood \leftarrow blood} = 3 \times 10^{-11} Gy.ml.Bq^{-1}s^{-1} = 108\ Gy.ml.GBq^{-1}.h^{-1}$.
- τ_{blood} [h.ml^{-1}] is the residence time per milliliter of blood for the activity concentration in the blood (activity normalized to the administered activity) (eq. 4);
- $S_{blood \leftarrow body}$ [Gy.GBq^{-1}.h^{-1}] is the S value used to estimate the contribution of the whole-body activity concentration to the absorbed dose to the blood. Only γ photon contributions are considered. $S_{blood \leftarrow body}$ is given by eq. 2.
- τ_{body} [h] is the residence time in the whole body (eq. 4).

$$S_{blood \leftarrow body} = \frac{0.0188}{wt^{2/3}}\ [Gy.GBq^{-1}.h^{-1}] \quad (2)$$

Here, τ_{blood} and τ_{body} were estimated from eq. 3 and $R(t)$, the fraction of the administered activity A_0 as a function of time, which is measured, respectively, by means of blood sample collection and whole-body acquisition:

$$\tau = \int_0^\infty R(t)\, dt \tag{3}$$

where $R(t)$ is the fraction of the administered activity A_0 as a function of time t. R(t) is measured for both blood samples ($R_{blood}(t)$) and whole-body acquisitions ($R_{body}(t)$) such that τ_{blood} and τ_{body} can be computed before estimating the dose from eq. 1.

As recommended (*16*), to determine $R_{blood}(t)$ (eq. 4), we repeatedly collected 2 ml of whole-blood samples during hospitalization in the nuclear medicine department. Whole-body measurements were also taken (counter: gamma counter Wallac, model wizard 1480, Wallacoy, Turku, Finland).

To determine the activity concentration of each sample, $A_{blood}(t)$, the number of counts per minute given by the gamma counter was first corrected from the background noise. Then, the activity per tube was determined from the known calibration factor of the well counter used. Finally, each value obtained was corrected for the physical decay of ^{131}I to account for the time between sampling and analysis and was finally used to compute $R_{blood}(t)$ with respect to the activity administered, eq. 4:

$$R_{blood}(t) = \frac{A_{blood}(t)}{A_0} \tag{4}$$

The whole-body fraction of the administered activity, $R_{body}(t)$, was determined from eq. 5 using a gamma counter located at a distance of two meters from the thyroid area. The patient sat on a stool so that the whole body was included in the solid angle of the counter (gamma counter: ATOMLAB 930 thyroid uptake system, Biodex Medical Systems, Inc., Shirley, NY, USA). Anterior and posterior acquisition of one minute each were considered for counting gamma photons in the range of [309 keV - 419 keV]:

$$R_{body}(t) = \left(\frac{WB_{counts}(t)}{WB_{counts}(t_0)}\right) \times e^{-\lambda_{131_I} \cdot t_0} \quad (5)$$

where $WB_{counts}(t_0)$ is the total number of counts at first acquisition, t_0 is the time of first acquisition, and t=0 is the time of activity administration.

In practice, different procedures describing the chronology, patient position, measurements, data collection, sample analysis and data recording were implemented in the nuclear medicine department. The different tasks were shared between nurses, medical physicists and radiopharmacists. Our chronology included blood sampling and body measurements before and 2 hours after iodine administration. Subsequently, blood and whole-body measurements were repeated at 6, 24, 40, 50, 72, 88 and 96 hours after administration of the iodine-131 capsule.

Table 1 summarizes the chronology of the different radioactive measurement tasks performed during the hospitalization period.

Posttreatment follow-up

Although thyroid cancer recurrence remains rare, most relapses occur within 5 years of diagnosis, but they may be delayed; thus, an extended follow-up period is required (*20*).

Surveillance is based primarily on cervical ultrasounds and serum levels of Tg (which normally becomes undetectable after ^{131}I ablative therapy in the absence of residual disease or recurrence) and levels of anti-Tg Abs.

In our population, the long-term therapeutic efficacy was evaluated clinically by regular endocrinological consultations, morphologically by cervical ultrasounds in the months following the administration of iodine (on average 9 months after) and biologically with regular monitoring of Tg, anti-Tg Ab and TSH levels. Chest scans were performed to morphologically monitor the presence of thyroid lung metastases. We did not perform systematic scintigraphy assessments in our population.

In parallel with monitoring therapeutic effectiveness, a surveillance of the possible toxicities, particularly hematological toxicities, was conducted. Specifically, to reflect these possible hematological toxicities at both the acute and chronic level, we recorded the short-term (approximately 2 to 6 months after radioiodine therapy), medium-term (approximately 1 year) and long-term (at the most recent follow-up) data for each patient.

RESULTS

Patients

We included 6 hemodialysis patients with thyroid cancer who underwent ^{131}I ablation. One of these patients received a second cycle of ^{131}I treatment (six months after the first treatment) due to metastatic bone disease. One patient was stage N+ during the initial extension assessment, and 2 were stage M+. The main characteristics of the patients are reported in Table 2.

Course of therapeutic management

The pretherapeutic thyroid stimulation for 5 patients consisted of an intramuscular injection of 0.9 mg recombinant human thyrotropin (rh TSH) 48 hours before capsule administration, and patient #2 had a THW one month prior to treatment (the administered activity and THW reported for patient # 2 in Table 4 was validated by the multidisciplinary team of the Gustave Roussy Institute).

The evolution kinetics of blood TSH in patients during their hospitalization is shown Fig.1, and the respective TSH values are shown in Table 3.

Note that patient #3 received two injections of Thyrogen® despite our recommendations, and patient #5, who had the highest TSH levels, did not fully adhere to her treatment and had a TSH baseline close to 400 microIU/mL.

All patients were hospitalized for 5 days in our department and received an average ^{131}I activity dose of 2603 MBq (median: 2274 MBq, range [1842 – 3747 MBq]). The two hemodialysis sessions

performed in our department were spaced two days apart; the majority of the sessions lasted approximately 4 hours, with an average total purified blood volume of 75 liters.

The main methods of ^{131}I administration and the main characteristics of the hemodialysis sessions are reported in Table 4 (except for patient #6, who had missing dialysis data).

Each patient underwent diagnostic scintigraphy performed 3 days after ^{131}I administration. Only one patient (patient #2 during his first treatment) had distant disease in the form of a bone metastasis on the rib cage (not confirmed by CT or MRI). The scintigraphy images of the anterior and posterior views and single-photon emission computed tomography (SPECT)-CT scan of this patient are shown Fig. 2.

The scans of the other 5 patients did not reveal any secondary focus.Regarding the exposure of staff members, the mean effective dose recorded with the operational dosimeter was 47.7 μSv [30.0-74.0] during the first session and 11.0 μSv [1.0-22.0] during the second session.

Evaluation of therapeutic efficacy

The results of clinical, biological (Tg, anti-Tg Ab, TSH) and ultrasound (thyroid ultrasound) follow-up tests confirmed the success of iodine-131 ablation treatment for 3 out of 4 patients classified as M0.

Patient #1 died of an intercurrent pathology (nonrevascularizable ischemic heart disease) shortly after ^{131}I treatment and was therefore unable to benefit from a long clinical-biological follow-up or thyroid ultrasound.

Twelve months after treatment, the Thyrogen test results of patient #4 showed a stimulated thyroglobulin value of less than 1 ng/ml. He underwent kidney transplantation in March 2015 and died 18 months later from infectious complications under immunosuppression.

In 2018, 1 year after ^{131}I treatment, the Thyrogen test of patient #3 confirmed biological remission with a stimulated thyroglobulin value of less than 1 ng/ml and the absence of anti-Tg Abs. The

patient struggled with compliance to hormonal treatment and had VACTERL syndrome, which causes malabsorption and high thyroid hormone requirements (7.5 µg/kg instead of 1.9 µg/kg Levothyrox) as well as difficulties in balancing TSH levels.

Patient #2, who had secondary bone lesions, benefited from a second ^{131}I administration. When performing whole-body thyroid scintigraphy on day 3 after the second administration, the bone lesions were no longer visible (Fig. 2).

Table 5 shows the results of the thyroid examinations performed before treatment and during the post-radioiodine therapy follow-up.

Assessment of therapeutic toxicity

None of the patients had any clinically significant side effects (including nausea, vomiting, dry syndrome, or salivary stones). To best reflect acute and chronic toxicities on hematopoiesis from a biological point of view, we performed blood tests shortly after ^{131}I administration (2 to 6 months later), 1 year later, and at the most recent follow-up visit. Over these time points, we did not find any significant decreases in the platelet and leukocyte counts or in hemoglobin levels, although this result remains difficult to interpret given the low values of hemoglobin in hemodialysis patients. The overview of blood counts before and after the patients received iodine therapy is reported in Table 6.

The kinetics of whole-body ^{131}I activity measured with a gamma counter over time are shown in Fig. 3. Table 7 presents the values of whole-body activity measured with a gamma counter before and after the two hemodialysis sessions in the protected area. The whole-body measurements of patient #6 were obtained with a gamma camera instead of a gamma counter (not available at the time of measurement).

Therefore, the whole-body activity was reduced on average by 66.7% [60.1-71.5] after the first dialysis and by 53.3% [30.4-67.8] after the second dialysis.

Fig. 4 shows the kinetics of blood activity measured via the various blood samples taken during hospitalization in the protected area.

The BM dose estimated by the method described in the EANM standard operating procedures (*16,18*) using the collected data (Fig. 3 and 4) averaged 0.992 Gy for all patients. The details of the estimated BM total absorbed doses of each patient are presented in Table 7.

The patients were discharged from the hospital with an estimated mean dose rate of 15.0 µSv /hour at 1 meter [7.0 µSv/hour -20.0 µSv/hour] and 5.8 µSv /hour at 2 meters [2 µSv/hour -10 µSv/hour].

DISCUSSION

The treatment of thyroid cancer with ^{131}I is intended to provide a sufficient dose to the residual thyroid tissue and/or secondary lesions while avoiding acute or subacute hematologic toxicity in patients with adequate renal function. Although patients #3 and #4 had a low recurrence risk, ^{131}I treatment was achieved because of a kidney grafting project requiring to minimize the risk of relapse as low as possible.

Finally, only one patient (patient #6) had an estimated BM total absorbed dose greater than 2 Gy. Prior to treatment, the patient benefited from a dosimetry evaluation (use of low activity to estimate the residence time of ^{131}I in the body with the same methodology). This pretherapy evaluation was achieved with two-way dialysis, and the BM dose was estimated to be 1.18 Gy for a prescription activity of 3700 MBq. Unfortunately, during the second stage of management for this patient, which was therapy, the first dialysis session was performed with one channel instead of the two channels used for the pretherapy evaluation, resulting in a decrease in the flow rate and, thus, in

the total purified blood volume. However, this patient did not exhibit any biological complications during follow-up.

In patients with end-stage renal disease, the spontaneous excretion of urine is very limited or totally absent, and the effective half-life of ^{131}I is more than four times higher in these patients than in patients with normal renal function (*15*). It is imperative that the use of ablative doses in these patients be paired with extrarenal purification to limit the dose to the hematopoietic marrow. This strategy is also recommended by the EANM Dosimetry Committee. However, the latter does not yet specify the standard dose to be administered, the radioactivity measurement methods to be used or the methods for performing hemodialysis sessions (*6*).

These results show that hemodialysis sessions for patients treated with iodine-131 are safely and effectively achievable in a shielded area within the nuclear medicine department. Clearly, a good facility infrastructure is mandatory to ensure the quality of the water as well as the quality of the effluent removal system in the decay tanks. In addition, good communication with the hemodialysis department and the dialysis nursing staff is needed to coordinate the use of mobile dialysis devices.

Unfortunately, the size of our population remains insufficient to draw conclusions, but a single dose of Thyrogen® allowed us to obtain satisfactory results in terms of thyrotropic stimulation while offering tangible comfort to the patients by avoiding the issue of hypometabolism related to THW. The residence time of ^{131}I in dialysis patients does not seem to be solely related to the thyrotropic stimulation modality but also to the rhythm and efficiency of the dialysis. Our small number of patients, including only one THW patient with a single distant bone lesion, does not allow us to compare the differences in irradiation according to the type of stimulation or the metastatic and nonmetastatic characteristics of the disease.

There are two general approaches to determine the appropriate ^{131}I dose to treat thyroid cancer. Individual dosimetry studies were performed according to previous studies (*8,21,22*) such as that by Hanscheid et al. (*23*), who incorporated an analysis based on the MIRD parameter, while others used empirical dose methods (*12,24-27*). In the latter group, some authors suggested reducing the amount of activity to avoid excessive radiation exposure (*12,26*), while others proposed increasing the amount of activity due to the rapid clearance of iodine with dialysis (*25,27*). A third point of view suggests that the dose should be the same as that in the population with normal renal function (*21,22*).

Because patient #6 received administered activity that was similar to the nominal activity and had an estimated BM total absorbed dose that was slightly greater than 2 Gy because of a dialysis exception, we continue to empirically reduce the administered activity of ^{131}I. This activity reduction has allowed nonmetastatic patients to meet the remission criteria while remaining safe in the event of slight deviations from the dialysis protocol.

For patient #2 with bone metastasis, a fixed activity of 3100 MBq also allowed for the elimination of the bone lesion without causing overirradiation.

Thus, we recommend a 30% reduction in activity from the nominal dose for ablative or adjuvant treatments in hemodialysis patients. However, for metastatic patients, the realization of a pretherapeutic dosimetry study is expected to refine the amount of activity to be administered. Notably, the dialysis sessions must be performed under the exact same conditions as those during the dosimetry studies achieved before or during the ^{131}I radiotherapy to avoid variations such as those in the case of patient #6. Indeed, for this patient, a different dialysis approach led to an erroneous final dosimetry computation, but no hematologic toxicity has been observed in the medium and long term.

The dialysis sessions limit whole-body overirradiation for the patient because of the low level of binding between proteins and iodine, which can be easily removed through hemodialysis membranes. However, the timing of these sessions needs to be correct to allow sufficient dialysis in order to prevent the accumulation of excessive irradiation while avoiding dialysis too early to eliminate too much iodine, which would reduce the efficacy (*8*).

Howard et al. (*24*) showed that for a patient on hemodialysis, the thyroid uptake is 6% at 24 hours and 10% at 48 hours. Therefore, waiting 42 hours after iodine administration for the first dialysis session seemed appropriate.

At patient discharge, the average dose rate at a distance of one meter was 15.0 μSv/hour. This figure is consistent with that found by other authors, such as Murcutt et al. (*28*), who observed an average dose of less than 20 and 18 μSv/h, respectively, at one meter when the patient was discharged from the hospital.

The patient's whole-body activity was measured before and after each hemodialysis session to assess the clearance of ^{131}I: the mean fraction of ^{131}I cleared in our population was 66.7% (range 60.1 - 71.5%) following the first session, which is consistent with the data reported by other authors that showed a clearance ranging from 50 to 72% (*8,25*).

The staff member with the most exposure was the dialysis nurse at the first session. The level of exposure was acceptable for a typically unexposed worker.

In contrast to patients with normal renal function, the ^{131}I elimination curve for renal failure patients on dialysis was not exponential. For this reason, the method we used to calculate the BM dose differs from that used for patients with normal renal function and allows for iodine clearance over a longer period of time requiring more blood samples and body measurements, especially before and after each dialysis session. None of the patients included showed any hematologic toxicity during short-, medium- and long-term follow-up periods.

Given the rarity of thyroid cancer in hemodialysis patients with renal insufficiency and the limited data in the current literature, we believe that reaching a formal consensus on the ideal management of these patients will be difficult. This situation will likely persist until a significant amount of dosimetry data are accumulated and new studies are undertaken. Finally, the fundamental intention of this study was not to suggest a new therapeutic model or to propose a dose optimization method for these patients but to aggregate data from several actual cases by proposing an effective dose tracking method.

CONCLUSION

Our treatment protocol with iodine-131 in patients with thyroid cancer undergoing hemodialysis was carried out safely and efficiently.

The treatment of thyroid cancer in patients with renal insufficiency who are undergoing hemodialysis requires a multidisciplinary approach involving endocrinologists, physicians, radiopharmacists, nurses and medical physicists, as well as nephrologists and a dialysis team.

This method for determining the absorbed dose might also be useful prior to therapy to determine the level of ^{131}I activity that should be administered, particularly for metastatic patients. However, this approach for determining the absorbed dose in the BM should be systematically applied for all patients both for monitoring and to ensure that the absorbed dose remains lower than the 2 Gy threshold for the BM.

KEY POINTS:

QUESTION: Is the management of patients who have end-stage renal disease and are undergoing hemodialysis alongside their radioiodine therapy achievable?

PERTINENT FINDINGS: From 2011 to 2018, 6 patients were treated in the metabolic radiotherapy unit after thyroid stimulation and with a dedicated protocol to assess the absorbed dose to the bone marrow. The administered activity was reduced by approximately 30%.

IMPLICATIONS FOR PATIENT CARE: The success of ablative treatment for the majority of patients with no significant hematologic toxicity confirmed the possibility of delivering ^{131}I treatment alongside hemodialysis.

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Day	Time from radioiodine administration	Task	Description
Day 1	0	Admission to the nuclear medicine dept after receiving dialysis in the hemodialysis area Micturition if the patient is able Administration of the radioiodine capsule	
	2 h (t1)	Whole-body acquisition Blood sampling (2 ml)	
	6 h (t2)	Whole-body acquisition Blood sampling (2 ml)	
Day 2	24 h (t3)	Whole-body acquisition Blood sampling (2 ml)	
Day 3	40 h (t4)	Whole-body acquisition Blood sampling (2 ml)	
	42 h (t5)	**Dialysis**	**First dialysis**
	50 h (t6)	Whole-body acquisition Blood sampling (2 ml)	
Day 4	72 h (t7)	Whole-body acquisition Blood sampling (2 ml)	
Day 5	88 h (t8)	Whole-body acquisition Blood sampling (2 ml)	
	90 h (t9)	**Dialysis**	**Second dialysis**
	96 h	Whole-body acquisition Blood sampling (2 ml)	

Table 1: Chronology of the different tasks performed

PATIENT NUMBER	AGE (IN YEARS), SEX	SURGERY	HISTOLOGY	TNM
1	67, F	TT + LND	Papillary carcinoma	pT3a(s)N0M0
2A	47, M	TT + LND	Papillary carcinoma	pT1b(s)N1bM1
2B	48, M	TT + LND	Papillary carcinoma	pT1b(s)N1bM1
3	62, F	TT	Papillary carcinoma	pT2(m)N0M0
4	63, M	TT	Papillary carcinoma	pT1(m)N0M0
5	29, F	TT + LND	Papillary carcinoma	pT3a(s)N0M0
6	71, M	TT + LND	Vesicular carcinoma	pT3a(s)N0M1

Table 2: Main characteristics of the patients. TT = total thyroidectomy; LND= lymph node dissection.

		Patient number						
		1	**2a**	**2b**	**3**	**4**	**5**	**6**
Time of measurement	**t1**	368	200	286	609	135	786	313
	t2	270	185	309	637	96	462	283
	t3	299	207	298	601	94	490	198
	t4	177	223	332	696	75	545	174
	t5	309	161	303	489	54	506	91
	t6	303	217	370	419	45	275	99
	t7	246	216	339	359	38	364	56
	t8	262	198	338	243	20	366	28
	t9	166	X	X	179	X	176	X

Table 3: Blood TSH values during hospitalization (in microUI/ml). X = missing data

Patient no.	^{131}I activity administered (MBq)	Thyroid stimulation	1st hemodialysis			2nd hemodialysis		
			Duration (h)	ABV (L)	Filtration rate (ml/min)	Duration (h)	ABV (L)	Filtration rate (ml/min)
1	2242	rh TSH	4	63.3	300	3,5	53	250
2A	2856	weaning	4	80	350	4	78.1	400
2B	3022	weaning	4	85.3	350	4	88.9	350
3	2274	rh TSH	4	80.1	350	4	82.4	350
4	1842	rh TSH	4	69.4	150	4	72	300
5	2243	rh TSH	4	71	330	4	75	350
6	3747	rh TSH	X	X	X	X	X	X

Table 4: ^{131}I activity administered, stimulation modality and characteristics of the dialysis sessions performed in the protected area. ABV = absolute blood volume; X = missing data

Patient number	Thyroid test the day of ^{131}I administration	Thyroid test after ^{131}I administration		
		≈ 2 to 6 months	1 year	most recent follow-up
1	Tgs: 0.17 Anti-Tg Ab: neg TSH: 368	Tg: X Anti-Tg Ab: X TSH: X	Tg: X Anti-Tg Ab: X TSH: X	Tg: X Anti Tg Ab: X TSH: X
2a	Tgs: 5.15 Anti-Tg Ab: neg TSH: 200	Tg: 0.51 Anti-Tg Ab: neg TSH: 0.06	see 2b	see 2b
2b	Tgs: 0.41 Anti-Tg Ab: neg TSH: 286	Tg: 0.1 Anti-Tg Ab: neg TSH: 0.94	Tg: 0.1 Anti-Tg Ab: neg TSH: 0.08	Tg: 0.1 Anti-Tg Ab: neg TSH: 0.04
3	Tgs: 0.17 Anti-Tg Ab: neg TSH: 609	Tg: < 0.15 Anti-Tg Ab: neg TSH: 2.28	Tg: 0.43 Anti-Tg Ab: X TSH: 0.768	Tgs: 0.63 Anti-Tg Ab: X TSH: 175
4	Tgs: 5.35 Anti-Tg Ab: neg TSH: 135	Tg: X Anti-Tg Ab: TSH: 0.32	Tgs: 0.2 Anti-Tg Ab: neg TSH: 69	Tg: 0.1 Anti-Tg Ab: neg TSH: 0.23
5	Tgs: 15.8 Anti-Tg Ab: neg TSH: 786	Tgs: 0.19 Anti-Tg Ab: neg TSH: 496	Tg: < 0.15 Anti-Tg Ab: neg TSH: 2.98	Tg: < 0.15 Anti-Tg Ab: neg TSH: 1.87
6	Tgs: 28.7 Anti-Tg Ab: neg TSH: 313	Tg: 20.8 Anti-Tg Ab: neg TSH: 0.67	Tg: 35 Anti-Tg Ab: neg TSH: 0.01	Tg: 170 Anti-Tg Ab: neg TSH: 0.06

Table 5: Thyroid assessments before and after treatment. Tg and stimulated thyroglobulin (Tgs) (ng/ml); TSH (microIU/ml); Anti-Tg Ab: neg = negative for anti-thyroglobulin antibodies; X = missing data

Patient number	Blood test before ^{131}I administration	Blood test after ^{131}I administration		
		≈ 2 months	≈ 1 year	most recent follow-up
1	Hb: 15.1 Pq: 155 000 Leuco: 9 230	Hb: 11.2 Pq: 162 000 Leuco: 7 800	Patient deceased	Patient deceased
2a	Hb: 9.4 Pq: 179 000 Leuco: 4 880	Hb: 12.1 Pq: 203 000 Leuco: 5 200	see 2b	see 2b
2b	Hb: 12.1 Pq: 175 000 Leuco: 5 980	Hb: 11.5 Pq: 199 000 Leuco: 3 800	Hb: 12.0 Pq: 216 000 Leuco: 6 500	Hb: 10.6 Pq: 208 000 Leuco: 5 000
3	Hb: 9.5 Pq: 218 000 Leuco: 5 880	Hb: 8.6 Pq: 171 000 Leuco: 3 760	Hb: 12.4 Pq: 173 000 Leuco: 4 670	Hb: 11.5 Pq: 212 000 Leuco: 4 570
4	Hb: 10.7 Pq: 255 000 Leuco: 5 310	Hb: 11.2 Pq: 268 000 Leuco: 5 570	Hb: 11.0 Pq: 251 000 Leuco: 4 700	Hb: 12.4 Pq: 274 000 Leuco: 6 230
5	Hb: 11.5 Pq: 141 000 Leuco: 4 120	Hb: 12.9 Pq: 155 000 Leuco: 5 800	Hb: 10.9 Pq: 96 000 Leuco: 2 500	Hb: 12.6 Pq: 150 000 Leuco: 5 420
6	Hb: 11.0 Pq: 172 000 Leuco: 5 640	Hb: 11.8 Pq: 223 000 Leuco: 6 400	Hb: 10.9 Pq: 212 000 Leuco: 7200	Hb: 10.7 Pq: 160 000 Leuco: 5 260

Table 6: Comparison of hematopoietic function before and after administration. Hb = hemoglobin (g/dL); Pq = platelets (/mm3); leuco = leukocytes (/mm3).

Whole-body activity, R(t)

Patient number		1	2a	2b	3	4	5	6
1st hemodialysis	before	0.744	0.767	0.747	0.720	0.641	0.882	0.65
	after	0.250	0.264	0.298	0.224	0.208	0.251	0.35
2nd hemodialysis	before	0.149	0.188	0.208	0.132	0.112	0.136	0.23
	after	0.048	0.091	0.100	0.054	0.078	0.056	0.11
Dose (Gy)		0.624	0.687	0.985	0.953	0.431	0.941	2.323

Table 7: Normalized whole-body activity measured with a gamma counter before and after dialysis and total absorbed dose to blood estimated from the measurement.

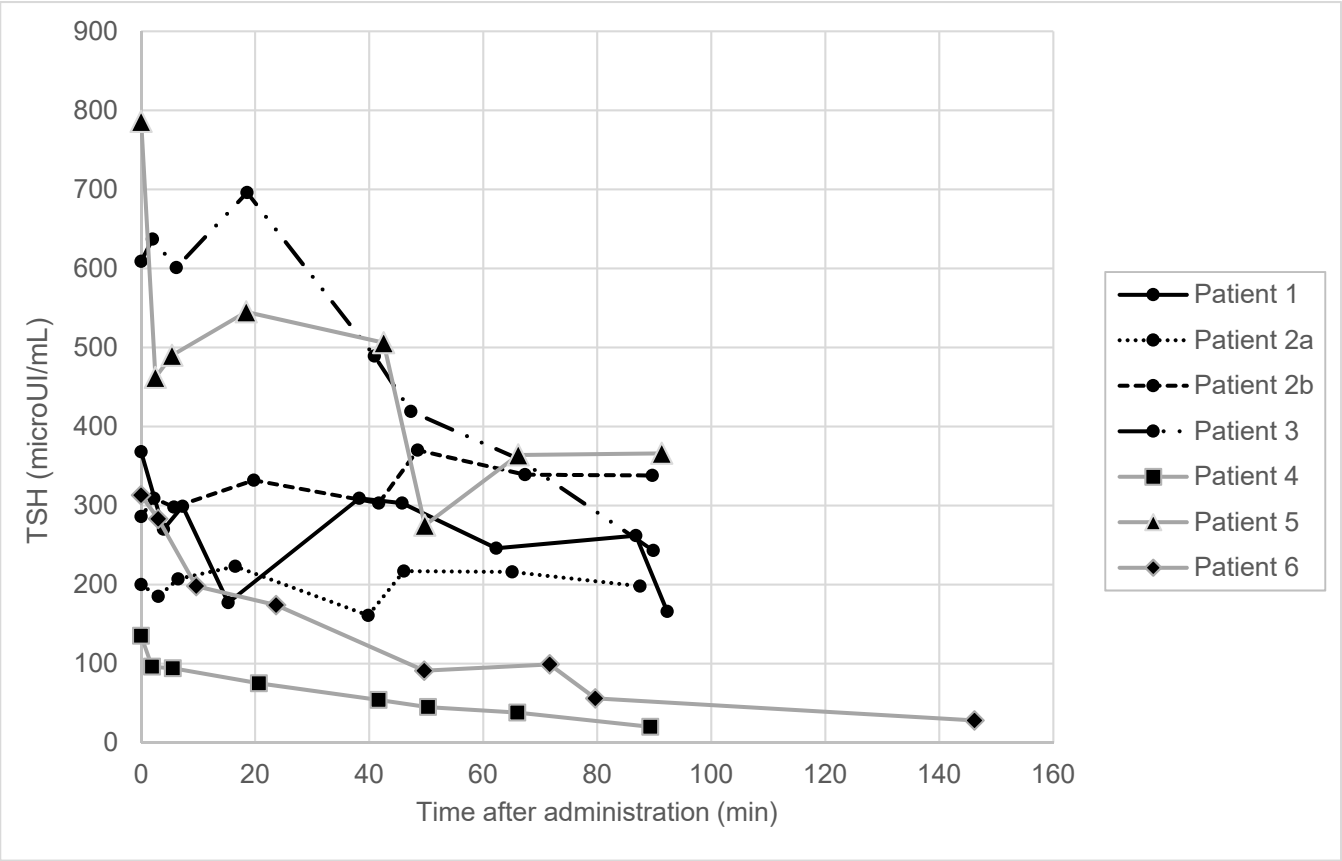
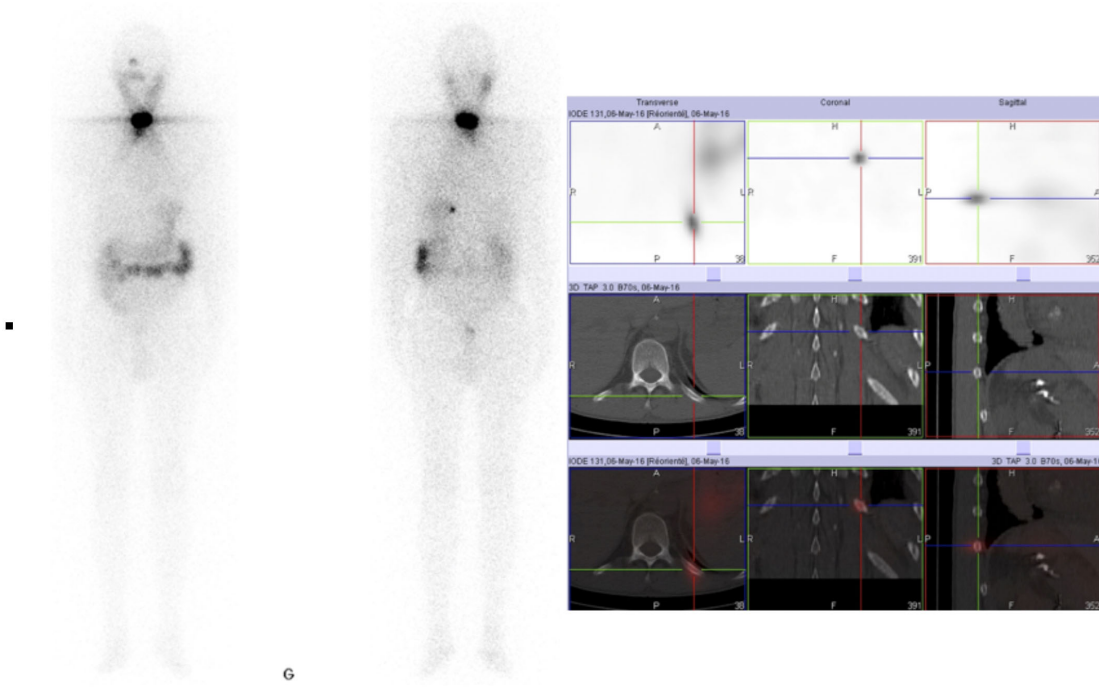


Figure 1: Kinetics of the blood serum TSH levels (in microIU/ml) during hospitalization. t(n) = time of the n^{th} TSH measurement during hospitalization (measured simultaneously with the dosimetry measurements)

A

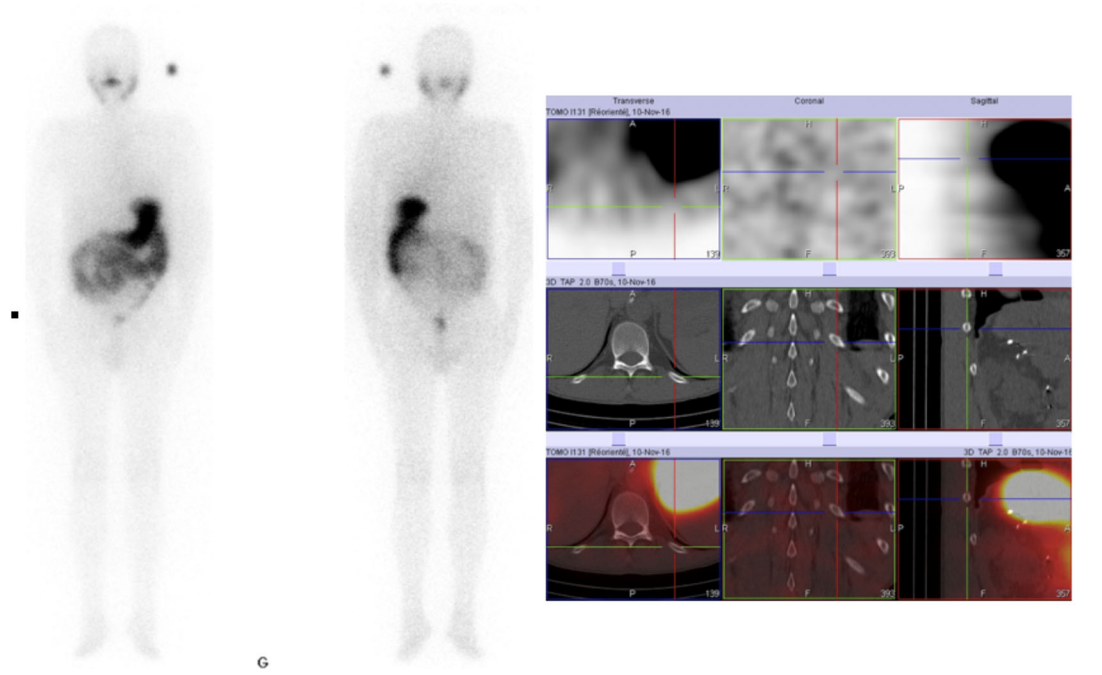
1st treatment: 2 856 MBq



(a)

B

2nd treatment: 3 022 MBq



(b)

Figure 2: Scintigraphy and ^{131}I SPECT-CT images of patient #2 after the first iodine administration (a) and the corresponding images at day 3 after the second administration (b), which show the disappearance of the metastatic focus on the left side of the 11th rib.

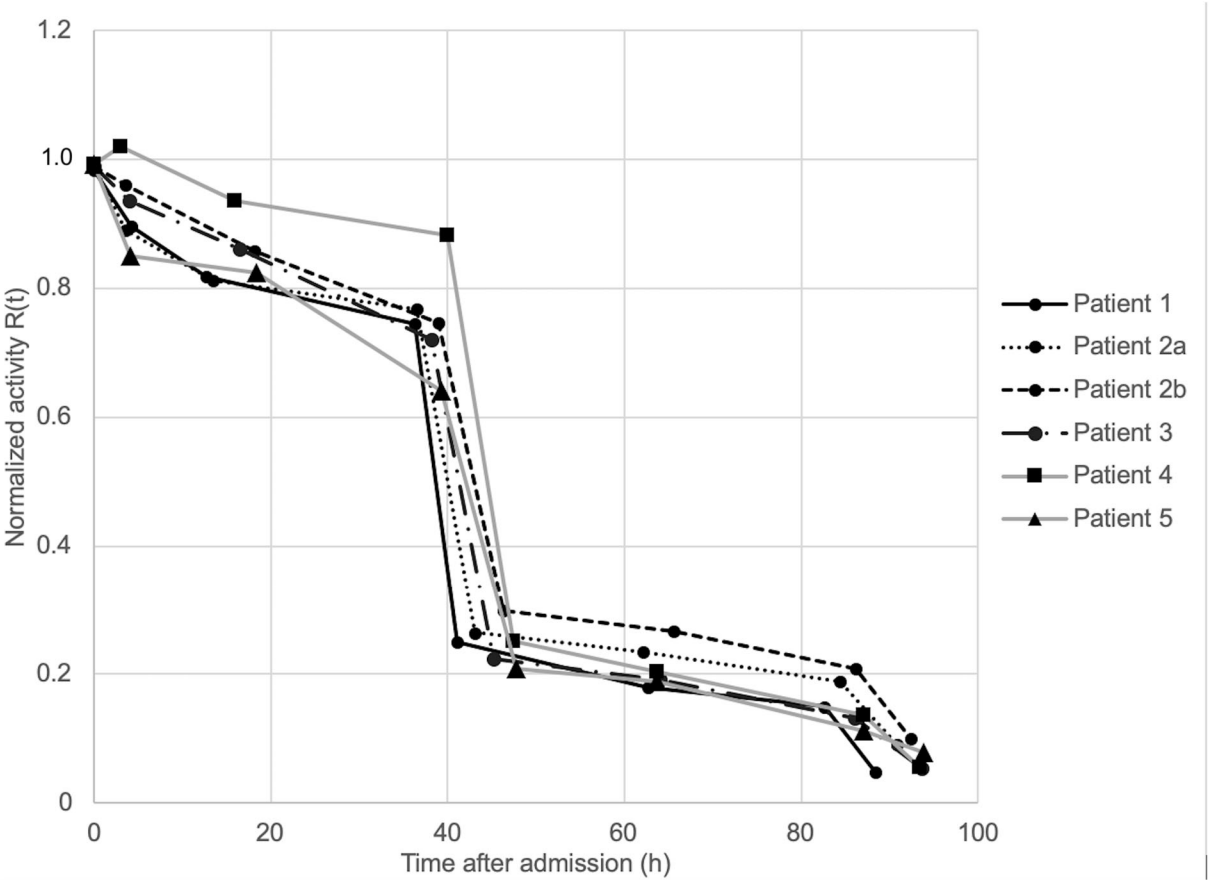


Figure 3: Normalized R(t) activity of the whole body as measured by a gamma counter as a function of time

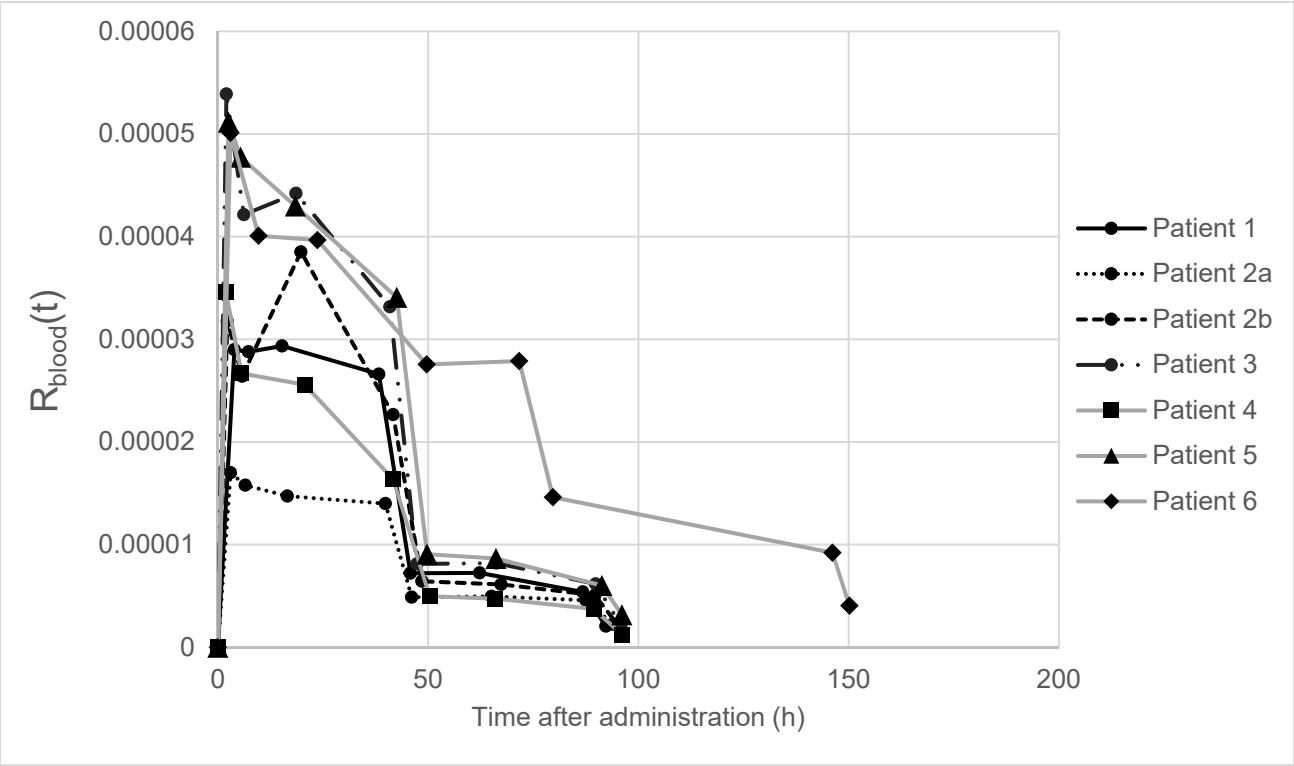


Figure 4: Normalized $R_{blood}(t)$ in for blood activity as a function of time (in hours)