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Contact restriction time after common nuclear medicine therapies: spreadsheet implementation based on conservative retention function and individual measurements

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E-mail: david.broggio@irsn.fr**Keywords:** contact restriction time, nuclear medicine therapies, public exposureSupplementary material for this article is available [online](#)

Abstract

The increasing use of new radiopharmaceuticals invites us to reconsider some radiation protection issues, such as the contact restriction time that limits public exposure by nuclear medicine patients. Contact restriction time should be patient specific and conservative, and its assessment made easy for clinicians. Here a method is proposed based on conservative estimation of the whole-body retention function and at least one measurement of the patient's dose rate. Recommended values of the retention function are given for eight therapies: ¹³¹I (Graves' disease, remnant ablation, patient follow-up, meta-iodobenzylguanidine), ¹⁷⁷Lu-prostate-specific membrane antigen and ¹⁷⁷Lu-DOTATATE therapies, and ⁹⁰Y and ¹⁶⁶Ho microsphere injection of the liver. The patient line source model for scaling dose rate from one distance to another is included in the restriction time calculation. The method is benchmarked against published values and the influence of the dose rate scaling and whole-body retention function illustrated. A spreadsheet is provided, along with the source code, with recommended values for the eight therapies. The recommended values can be changed as well as the dose rate scaling function, and other radiopharmaceuticals can be included in the spreadsheet provided retention functions are defined.

1. Introduction

After several decades of domination by radio-iodine treatment, nuclear medicine is evolving fast. This evolution is driven by the improvement in and availability of imaging devices and the development of new therapeutic radiopharmaceuticals, potentially combined with companion diagnostic agents in the so-called theranostic approach (Levine and Krenning 2017). Numerous clinical trials are ongoing; ¹³¹I, ¹⁷⁷Lu and alpha emitters are being tested, coupled to a variety of vectors targeting cancer cells (Sgourous *et al* 2020). The novelty and success of therapies, the renewed interest of the pharmaceutical industries (Sherman and Levine 2019) and the reimbursement of some therapies has led to an increase in the number of patients being treated, and this trend is expected to continue (Czernin *et al* 2019).

This situation invites us to reconsider radiation protection issues in nuclear medicine, which covers radionuclide production, exposure of staff, patients and members of the public, waste management and even handling of corpses and cremation (ICRP 2019, Martin *et al* 2019, European Commission 2020, Kyriakidou *et al* 2021).

General guidance is available regarding the protection of members of the public potentially exposed by patients. The IAEA (2009) provides tables giving discharge criteria or restriction contact times for various radionuclides, either as a function of measured dose rate or activity retained in patients. The tables provided by the IAEA are extracted or adapted from different sources, including national or international guidance (European Commission 1998, ICRP 2004), which do not include recent radiopharmaceuticals nor recent

data or methods. Patients' excreta also represents a potential source of contamination of patients' relatives and special precautions should be taken for some radiopharmaceuticals that are mainly excreted through urine or faeces, such as ^{89}Sr or ^{223}Ra (ICRP 2019).

Discharged patients should receive information on the duration of contact restriction with family members and relatives or members of the public to limit their exposure (Council of the European Union 2014, Demir *et al* 2016). Given a scenario consisting of exposure times and distances and assuming a multi-exponential dose rate, the general method for calculating restriction time has been given by Cormack and Shearer (1998) who considered multiple contact intervals of varying durations. The case of multi-exponential dose rate was also considered in Zanzonico *et al* (2000) but the contact duration was described by the exposure factor, i.e. the daily proportion of time that the patient spends at a given distance from the exposed person (thus contact intervals are not explicitly used in calculations). The case of mono-exponential decay has been treated in Carlier *et al* (2004), who considered that all contact intervals, whatever the scenario, started at the patient discharge time and were periodical.

In these three approaches it was acknowledged that a radiopharmaceutical-specific model of the temporal variation of the dose rate from the patient is necessary but not sufficient, and one or several measurements of the patient's dose rate are needed. The patient's dose rate is proportional to the whole-body activity and thus biokinetic models can, in principle, be used to calculate it. However, first the calculation is not straightforward, unless the exposure rate constant is used and thus the point source approximation. Second, whole-body or organ activity are highly variable: illustrative examples can be found in Kurth *et al* (2018), Mair *et al* (2018), Levart *et al* (2019) and Bellamy *et al* (2022) for lutetium therapy and in Berg *et al* (1996), Areberg *et al* (2005) and Hänscheid *et al* (2006) for radio-iodine therapy. As such, measurements of the patient dose rate merely serve as a normalisation of the dose rate pattern given by biokinetic models.

The exposure scenarios usually consider several contact distances where the dose rate has not been measured and correction factors are thus needed. This problem is avoided in Zanzonico *et al* (2000) where the dose rate is measured at the two required distances. For iodine therapy it is considered in Carlier *et al* (2004) that dose rate varies as the inverse of distance, while in Cormack and Shearer (1998) this inverse distance scaling is applied for all radiopharmaceuticals. The US Nuclear Regulatory Commission (NUREG 2019) still recommends calculating discharge criteria based on the point source approximation and thus an inverse square law scaling. However, it has been illustrated in several studies that approximating the patient as a line source gives exposure calculations in better agreement with experimental data (Siegel *et al* 2002, De Carvalho *et al* 2011, Yi *et al* 2013). Recently a spreadsheet implementing the Zanzonico approach was issued for the case of remnant ablation, the inverse square law scaling was applied and the source code is protected (Han *et al* 2021). Another spreadsheet implementation has been proposed in Otis (2020): the inverse square law is compensated by ad hoc correction factors and the user has to change the restriction time step by step until the exposure falls below the dose constraint.

In this work, the case of conservative bi-exponential whole-body retention and of dose rate measurements at the patient discharge date is considered. An explicit formula is derived for the calculation of the restriction duration, with the exposure scenario defined by exposure durations and distances, following the Carlier approach (Carlier *et al* 2004). The formula introduces a dose rate scaling factor to take into account several exposure distances and guidance is given for the choice of this factor. Calculation examples are given for radioiodine and lutetium therapy, they illustrate the influence of the scaling factor and of the whole-body retention function. A calculation spreadsheet is provided to carry out the calculation. The spreadsheet includes recommended input parameters for eight therapy cases, based on recent literature data; other cases can be easily defined by the user.

2. Material and methods

An explicit formula to calculate contact restriction time is derived. Exposure scenarios are defined by the times and distances of contact between discharged patients and members of the public. An exposure scenario applies to a specific category of members of the public (pregnant women, children, etc) and is thus associated with a dose constraint. The dose rate due to the patient is integrated over exposure periods to find the time at which contact restriction can be relaxed. The dose rate is assumed to be proportional to the radiopharmaceutical retention but scaled to dose rate measurements. Since dose rate measurements are not necessarily carried out at distances considered in the exposure scenario the problem of distance correction is also taken into account.

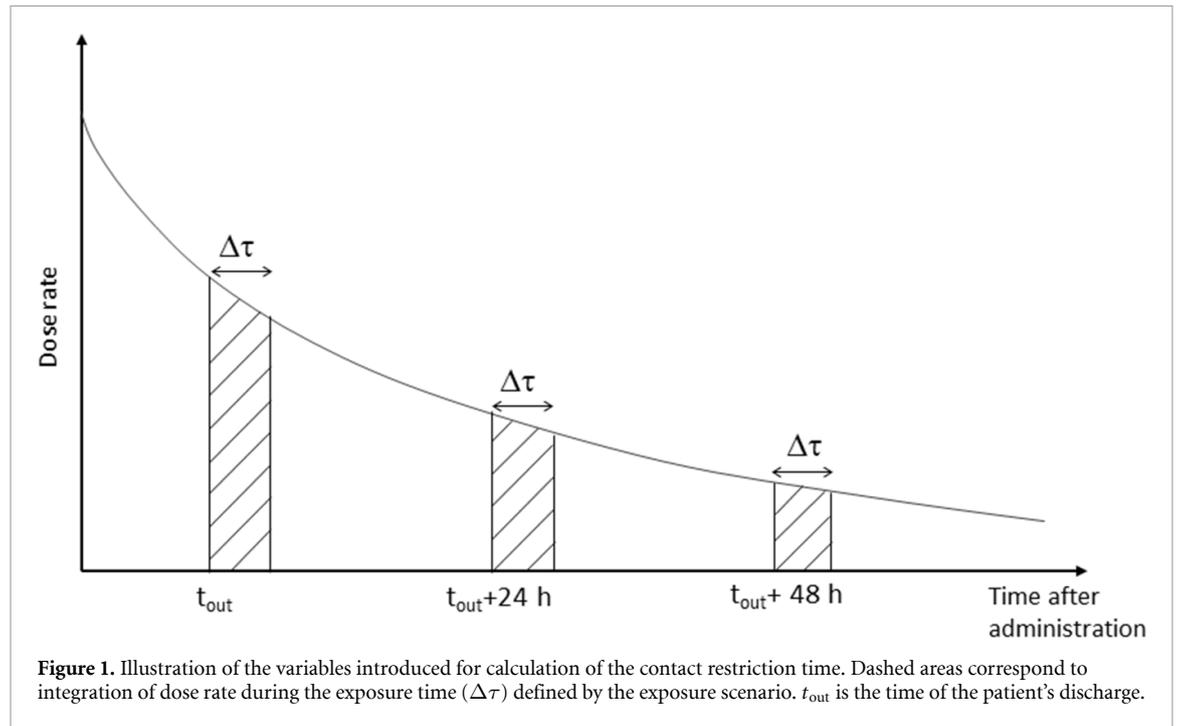
2.1. Exposure scenario

Exposure scenarios are needed to define the time and distance spent nearby different categories of people once the patient is discharged. For each category of people, a dose constraint can be set to limit its exposure.

Table 1. Typical contact scenarios for calculation of contact restriction time.

Case	Situation	Daily time and distance of contact	Dose constraint (mSv)
A	Contact with partner	8 h at 0.3 m and 6 h at 1 m	3 ^a
B	Contact in public transportation	30 min at 0.1 m	0.3
C	Contact with a child (<2 years old)	9 h at 0.1 m	1
D	Contact with a child (≥2 and <5 years old)	4 h at 0.1 m and 8 h at 1 m	1
E	Contact with a child (≥5 and <11 years old)	2 h at 0.1 m and 4 h at 1 m	1
F	Contact with a pregnant woman	6 h at 1 m	1
G	Contact with work colleagues	8 h at 1 m	0.3

^a In Carlier *et al* (2004) 3 and 15 mSv are proposed depending on the age of the partner. Here 3 mSv is retained.



Professionals and regulators can define these scenarios; here the scenarios given in Carlier *et al* (2004), which are based on scenarios defined in Barrington *et al* (1996), are considered. An exposure scenario, for a category of people, can consist of several contact times and distances, as summarised in table 1.

2.2. Cumulated exposure and dose constraint for a mono-exponential dose rate

Let us assume that the dose rate, at a given distance from the patient, is known, and decays following a single exponential:

$$\dot{D}(t) = a_0 \exp(-\lambda t). \tag{1}$$

With this notation it is implied that a_0 is in fact a function of the distance, but this variation is first disregarded and will be taken into account later. Hereafter the unit of time is hours.

Let us then consider that the patient is discharged at a time t_{out} and that contact will occur every 24 h for a duration $\Delta\tau$ at the distance for which the dose rate is known. Figure 1 illustrates the variables introduced for the calculation.

We look for the date after which summation of integrated dose rates is less than the dose constraint (D_{con}) defined by the scenario. This reads

$$\sum_{k=n}^{\infty} \int_{t_{out}+k*24}^{t_{out}+k*24+\Delta\tau} \dot{D}(t) dt \leq D_{con}. \tag{2}$$

In this equation one must find n , i.e. the number of days after which the doses due to subsequent contacts will never exceed the constraint.

In case of a mono-exponential decay, the summation can be written explicitly, and the following result is obtained:

$$\frac{a_0}{\lambda} \frac{(1 - e^{-\lambda \Delta t})}{1 - e^{-24 \cdot \lambda}} e^{-\lambda t_{\text{out}}} e^{-n \cdot 24 \cdot \lambda} \leq D_{\text{con}}. \quad (3)$$

In this approach, it is conservatively assumed that daily contacts, whatever the scenario, take place every 24 h after the patient discharge time.

2.3. Cumulated exposure and dose constraint from whole-body retention and dose rate measurement

Let us now assume that the whole-body retention, $R(t)$, is known and consists of two exponential terms describing a short and long phase of retention (the general case of several exponentials could be considered, but in practice one can rarely specify the whole-body retention with more than two components):

$$R(t) = A_s \exp(-\lambda_s t) + A_l \exp(-\lambda_l t). \quad (4)$$

The retention is the fraction of injected activity that remains in the whole body at a given time; A_s and A_l sum to one.

We then assume that the dose rate due to the patient is proportional to the whole-body retention and further consider that the dose rate at a reference distance has been measured at t_{out} ($\dot{D}_{\text{out}}(d_{\text{ref}})$). The dose rate variation, at the reference distance, can thus be given as a function of the whole-body retention

$$\dot{D}(t) = \frac{R(t)}{R(t_{\text{out}})} \dot{D}_{\text{out}}(d_{\text{ref}}). \quad (5)$$

This last expression ensures that the dose rate considered for calculation is proportional to the whole-body retention and is equal to the measured dose rate at the discharge time.

2.4. Distance correction and final relation

The exposure scenario can involve contact distances (d) that are different from the reference distance at which dose rate measurement has been performed. One thus must correct equation (5) to obtain the dose rate at the needed distances. This can be carried out by introducing a scaling factor $k(d, d_{\text{ref}})$

$$\dot{D}(t, d) = k(d, d_{\text{ref}}) \frac{R(t)}{R(t_{\text{out}})} \dot{D}_{\text{out}}(d_{\text{ref}}). \quad (6)$$

In the case of the point source approximation the scaling factor is simply $(d_{\text{ref}}/d)^2$. It turns out that a more suitable scaling factor is obtained if the patient is considered as a line source, and in this case there is an analytical formula for the scaling factor.

Putting the expression for $R(t)$ in equation (5) and using the result that has been obtained for mono-exponential decay in equation (3), the final expression that must be solved is

$$D_{\text{con}} \leq \frac{k(d, d_{\text{ref}})}{R(t_{\text{out}})} \dot{D}_{\text{out}}(d_{\text{ref}}) \left\{ \frac{A_s}{\lambda_s} e^{-\lambda_s t_{\text{out}}} \frac{(1 - e^{-\lambda_s \Delta \tau})}{1 - e^{-24 \cdot \lambda_s}} e^{-n \cdot 24 \cdot \lambda_s} + \frac{A_l}{\lambda_l} e^{-\lambda_l t_{\text{out}}} \frac{(1 - e^{-\lambda_l \Delta \tau})}{1 - e^{-24 \cdot \lambda_l}} e^{-n \cdot 24 \cdot \lambda_l} \right\}. \quad (7)$$

To summarise, in this equation

- the unknown quantity is n ; this gives the number of days after which restriction can be relaxed,
- four parameters (A_s , A_l , λ_s , λ_l) come from the whole-body retention equation
- $\Delta \tau$, d are fixed by the exposure scenario
- D_{con} is the dose constraint applying to a specific person
- $\dot{D}_{\text{out}}(d_{\text{ref}})$ is fixed by the dose rate measurement
- t_{out} is the discharge time.

When the scenario involves two distances and two contact times (cases A, D, E of table 1), the right-hand side of equation (7) must be calculated twice.

It can be noticed that if the decay is mono-exponential, equation (7) becomes independent of t_{out} . Indeed, in such a case one can consider t_{out} as the origin of time with an initial dose rate fixed by the measurement. On the contrary, if the model is bi-exponential it matters if t_{out} rather the short or long phase of the retention.

3. Results and discussion

3.1. Recommended whole-body retention function and scaling functions

Parameters of whole-body retention are recommended for four cases of ^{131}I therapy [remnant ablation, follow-up after remnant ablation, Graves' disease, meta-iodobenzylguanidine (mIBG) therapy], for ^{177}Lu -DOTATATE therapy, for ^{177}Lu -prostate-specific membrane antigen (PSMA) therapy and for liver therapy with ^{90}Y and ^{166}Ho microspheres].

The whole-body retention parameters for remnant ablation and follow-up are taken from Liu *et al* (2014). They were obtained from at least six dose rate measurements between 30 min and 144 h on 36 patients (ablation) and 41 patients (follow-up). The retained half-lives correspond to the upper 95th percentiles. The mean effective half-lives for the thyroidal compartment (i.e. the longer half-life) were in good agreement with previous studies (see discussion in from Liu *et al* (2014)).

The whole-body retention parameters for Graves' disease are taken from a companion study (Liu *et al* 2015). The retained half-life also correspond to upper 95th percentiles. To derive these values, measurements were taken from 72 patients with Graves' disease. The mean effective half-life was in good agreement with previous studies.

Whole-body retention data for mIBG treatment are relatively rare. In the supplementary material (A, part 1) the models provided in ICRP (1988), Tristam *et al* (1996) and Willegaignon *et al* (2018) and data provided in Ertl *et al* (1987) and Cougnenc *et al* (2017) are compared. A mono-exponential decay described by the upper 95th percentile of the effective half-life provided in Willegaignon *et al* (2018) was retained since it was conservative compared with other data.

Whole-body retention data for ^{177}Lu -DOTATATE can be found in Calais *et al* (2014), Mair *et al* (2018) and Levart *et al* (2019). Considering four patients and urine measurements, Calais *et al* derived the whole-body retention up to 5 h after therapy, from which an effective half-life of 5.3 h can be deduced. Considering 40 patients and planar imaging data up to 90 h after therapy, Mair *et al* considered the average over patients and provided the effective half-lives of a bi-exponential model: 2.5 and 63 h. Levart *et al* carried out planar imaging of 16 patients up to 168 h after ^{177}Lu -DOTATATE administration. They provided explicit bi-exponential models for the average of patients and examples for patients with slow and fast excretion. Here their example for slow excretion was retained, the fast and slow effective half-lives are 7.4 and 95.6 h, respectively.

The effective half-life of the slow component of ^{177}Lu -PSMA-617 whole-body retention is given, or can be calculated, from data provided in Baum *et al* (2016), Demir *et al* (2016), Kurth *et al* (2018), Mair *et al* (2018), FDA (2020) and Schuchardt *et al* (2022). Consistent values between 35 and 42 h are found (see table A.1 in the supplementary information), but they concern the average over a population. Considering 30 patients imaged for up to 118 h, Baum *et al* gave a maximum half-life (slow component) of 91 h. Using the distribution of effective half-life assessed from measurements at 48 h of the dose rate of 50 patients provided by Kurth *et al*, the 95th percentile of effective half-life can be estimated at 78 h. In FDA (2020) the geometric mean and geometric coefficient of variation of the effective half-life (slow component) are provided: assuming a log-normal distribution the 95th percentile can be calculated as 98 h. In Kurth *et al* (2018), Mair *et al* (2018) and FDA (2020) it is shown or stated that the whole-body retention is bi-exponential, but none of the references above provided data enabling to a 95th percentile or maximum bi-exponential model to be set up. Data from Kurth *et al* (2018) and Mair *et al* (2018) were tentatively extracted to fit a bi-exponential model, but the resulting effective half-lives of the slow component were too inconsistent with the 95th or maximum half-life given above. Consequently, for whole-body retention the values retained for ^{177}Lu -DOTATATE were adopted. At least the effective half-life of the slow component (95.6 h) is consistent with the 95th or maximum half-life given above.

Regarding liver therapy with ^{90}Y or ^{166}Ho , which are injected as microspheres and not eliminated from the liver, the physical decay only has to be considered.

In Broggio (2022) it was shown that the line source model correctly describes the scaling function needed to compute the dose rate at a given distance from a measurement at a reference distance, even in the case of remnant ablation or benign thyroid disease. More precisely it was shown that the patient height needed in the line source model to fit at best the scaling function can be considerably greater than usual patient height, but using a standard adult height of 176 cm instead of the fitted source line produces an approximation within 25%. The case of liver therapy was not considered in Broggio (2022). In Courneane *et al* (2019) the dose rate of 30 patients treated with TheraSphereTM was measured at three different distances, and it was shown that the dose rate variation with distance could be described by a power law with an exponent of -1.58 . It was thus investigated to what extent this trend could be approximated by an inverse square law or the line source model with standard adult height. In figure A.2 in the supplementary material it is shown that the line source model and power law produce scaling factors within 15%, when the dose rate is measured at 1

Table 2. Summary of recommended parameters describing whole-body retention and recommended distance scaling method.

Therapy	A_s	T_s (h)	A_l	T_l (h)	Distance scaling method
^{131}I , remnant ablation	0.98	16	0.02	120	Line source model
^{131}I , cancer follow-up	1	15	—	—	Line source model
^{131}I , Graves' disease	0.2	7	0.8	169	Line source model
^{131}I , mIBG treatment	1	33.8	—	—	Line source model
^{177}Lu -DOTATATE	0.44	7.4	0.56	95.6	Line source model
^{177}Lu -PSMA	0.44	7.4	0.56	95.6	Line source model
^{90}Y , liver therapy	1	64	—	—	Line source model
^{166}Ho , liver therapy	1	26.8	—	—	Line source model

READ THE DISCLAIMER AND INSTRUCTION SHEET BEFORE USING
Sheet for follow-up of thyroid cancer patient with ^{131}I

BIOKINETIC PARAMETERS for ^{131}I , follow-up
It is not recommended to change these values
For mono-exponential decay define T_{short} and A_{short} and leave T_{long} and A_{long} empty

T_{short} (hours) A_{short} (unitless)

T_{long} (hours) A_{long} (unitless)

1

INPUT HERE MEASUREMENT DISTANCES AND DOSE RATES AT PATIENT DISCHARGE
- at least one distance and dose rate pair
- at most five pairs

distance (meter)	<input type="text" value="1"/>	<input type="text" value="0.3"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
dose rate (micro-Sv/hour)	<input type="text" value="280"/>	<input type="text" value="1400"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

2

INPUT HERE DISCHARGE TIME
relative to radiopharmaceutical administration

discharge time relative to administration (hours) 3

Select distance scaling method 4 **Line source option is recommended**

5

RESTRICTION TIME CALCULATION
- Default scenarios are provided
- you can create new ones, taking the existing ones' as example (copy and modify the lines)
- scenarios are defined by "distance", "contact time", "dose constraint"

Scenario description	Dose constraint (mSv)	contact time #1 (hours)	distance #1 (meter)	contact time #2 (hours)	distance #2 (meter)	Contact restriction time (days)
Contact with partner	3	8	0.3	6	1	2
Travel in public transport	0.3	0.5	0.1			3
Contact with child (age < 2 years)	1	9	0.1			4
Contact with child (2 ≤ age < 5)	1	4	0.1	8	1	4
contact with child (5 ≤ age < 11)	1	2	0.1	4	1	3
Contact with pregnant woman	1	6	1			1
Contact with co-workers	0.3	8	1			3
Other scenario as example	1	8	0.3			3

6

Figure 2. Illustration of the calculation spreadsheet. (1) Definition of the whole-body retention function that can be modified even if not recommended. (2) Input of measured dose rates and measurement distance, (3) input of time of discharge, (4) selection of model for dose rate scaling, (5) predefined scenarios of exposure that can be modified or copied for modification, (6) automatic calculation and update of contact restriction time.

m and scaled between 30 and 300 cm. Comparatively a scaling with an inverse square law would produce an overestimation of 65% at 20 cm and an underestimation of 40% at 300 cm. It was thus considered that the line source model is a correct approximation for dose rate scaling and it is also adopted for ^{166}Ho therapy.

Recommended parameters for whole-body retention functions and scaling method are summarised in table 2. For better readability, the effective half-life rather than the decay constant appearing in equation (7) is given.

3.2. Spreadsheet implementation

The calculation of contact restriction time given by equation (7) and scenarios given in table 1 were implemented in an Excel file using VBA macros. More precisely, the Excel file consists of a disclaimer and instruction sheet and of eight sheets for each of the therapies described above. The file is provided as part B of the supplementary material.

All sheets are built similarly, they only differ by the parameters describing the whole-body retention function. Each sheet consists of three parts (see figure 2).

In the first part, the parameters describing the whole-body retention function are given as in table 2. The user can change these parameters even if it is not recommended (step 1 in figure 2).

In the second part (steps 1–3 in figure 2), the user must (i) enter at least one measurement distance and the corresponding dose rate, (ii) enter the discharge time (supposed to be the same as the measurement time) and (iii) select the distance scaling method. Up to five pairs of distance and dose rate values can be entered. If several measurement distances are given, the dose rate at the scenario distance will be scaled using the closest measurement distance (if there are two closest distances the smaller one is used). The line source model is described as recommended in all sheets, but the user is free to select the inverse square law (the dose rate varies like the inverse of squared distance) or inverse law (the dose rate varies like the inverse of the distance).

Table 3. Benchmark of calculation results for remnant ablation with ^{131}I (columns 2 and 3) and influence of the scaling function on the restriction time calculation (last columns). Scenario description and reported restriction times are taken from Liu *et al* (2014).

Scenario ^a	Restriction time (d) reported in (Liu <i>et al</i> 2014)	Calculated restriction time (d) using two measurement distances (this work)	Calculated restriction time (d) using only dose rate at 1 m (this work)		
			Line source model	Inverse square law	Inverse law
Sleep with nonpregnant adult family member for 8 h at 0.3 m (5 mSv)	1	1	1	2	1
Sleep with pregnant woman, infant or child for 8 h at 0.3 m (1 mSv)	3	3	4	6	3
Contact with nonpregnant adult family member for 6 h at 1 m (5 mSv)	0	0	0	0	0
Contact with pregnant woman, infant or child for 6 h at 1 m (1 mSv)	0	1	1	1	1
Contact with co-worker or member of the public for 8 h at 1 m (1 mSv)	1	1	1	1	1
Daytime contact with nonpregnant adult family member for 6 h at 1.0 m, followed by sleeping for 8 h at 0.3 m (5 mSv)	1	1	1	2	1
Daytime contact with pregnant woman, infant or child for 6 h at 1.0 m, followed by sleeping for 8 h at 0.3 m (1 mSv)	3	4	4	6	3

^a The dose constraint is given in parentheses after the exposure scenario description.

The third part consists of predefined scenarios, those of table 1, and upon changes of input parameters (distance and dose rate, discharge time) or scenario parameters, the contact restriction times are automatically updated. An additional scenario is provided as an example. As many scenarios as needed can be defined by copying and pasting the complete line defining a scenario. The only restriction is that a scenario can accommodate at most two contact durations and two contact distances.

Input parameters are checked before calculation; for example it is checked that A_{long} and A_{short} sum to one, that input values are numeric and positive, that measured dose rates and distances come in pairs, etc.

If one needs to define new sheets (for other radionuclides or to modify existing biokinetic parameters) it is advised to copy an existing sheet rather than modify existing ones.

The source code is included with the Excel file and can be modified.

3.3. Comparison with literature data

The data given in Liu *et al* (2014) were considered and the reported duration of contact restriction was compared with our calculations. For that purpose, we considered the case of remnant ablation with 3.7 GBq of ^{131}I and the given 95th percentile initial dose rates at 0.3 and 1 m, respectively 0.206 and $0.041 \mu\text{Sv h}^{-1}\text{MBq}^{-1}$. The contact scenarios considered in Liu *et al* (2014) are not those of table 1, they are given in table 3 with the reported durations of contact restriction and our evaluation. The two calculations only differed for two scenarios, for which an excess of 1 d was found. For the fourth scenario an exposure of 1.3 mSv was calculated if contact was not restricted and an exposure of 0.5 mSv if the contact restriction was 1 d. For the seventh scenario an exposure of 1.1 mSv was calculated if contact restriction was 3 d and 0.54 mSv if it was 4 d.

Our calculations were also compared with those given in Levart *et al* (2019) considering the reported data for inpatients and their ‘Mallinckrodt’ case. Patient discharge at 18.1 h and 95th percentile dose rate at

Table 4. Benchmark of calculation results for treatment with ^{177}Lu -DOTATATE. Scenario description and reported results are taken from Levart *et al* (2019).

Scenario	D_{con} (mSv)	Reported restriction time (d) (Levart <i>et al</i> 2019).	Calculated restriction time (d), this work
Contact with partner: 6 h at 1 m and 8 h at 0.1 m	1	15	16
Child (age <2 years): 8.75 h at 0.1 m	1	16	16
Child (2 < age < 5): 4 h at 0.1 m and 8 h at 1 m	1	13	12
Child (5 < age < 11): 2 h at 0.1 m and 4 h at 1 m	1	9	8
Co-worker: 8 h at 1 m	0, 3	5	5

0.1 and 1 m of, respectively, 334 and $15 \mu\text{Sv h}^{-1}$ were thus considered. As for the above example the results are given in table 4. For the five exposure scenarios considered in Levart *et al* (2019) our assessment is always within 1 d of the reported values. This might be attributed to the fact that contact restriction times in Levart *et al* (2019) are based on patient-specific data (biokinetic, exact discharge date, dose rates) and the 95th percentiles of contact restriction are reported, while in our calculation a single retention function and 95th percentile dose rates are used.

3.4. Influence of scaling factors and biokinetics

To illustrate the influence of the scaling function enabling correction of dose rate measurements from one distance to another, the example of remnant ablation provided in Liu *et al* (2014) was considered again. Instead of carrying out the calculations with the two dose rate measurements, the dose rate measurement at 1 m only was retained. Having this measurement, the three options for the scaling function were considered and the restriction times were recalculated, as reported in table 3. The line source model option produced the same results as when two dose rate measurements were used except for the second scenario ('Sleep with pregnant woman ...') where the restriction time was increased by 1 d. Using the inverse square law increased the restriction time for four scenarios and did not affect the other three. The three unaffected scenarios are those in which only the dose rate at 1 m is needed. For the other scenarios the dose rate at 0.3 m is needed, and using the inverse square law instead of the line source model increased the restriction times by 1 or 2 d. Using the inverse law instead of the line source model reduced the restriction time by 1 d for the last scenario only ('Daytime contact with pregnant woman ...').

It is important to examine the effect of attributing to all patients a conservative retention function and to see if taking into account the dose rate measurement is indeed effective in correcting for this bias. To gain insights into that question the cases of slow, mean and fast excretion described in Levart *et al* (2019) were considered. Taking the dose rates considered above for the slow excretion function, the expected dose rates for mean and fast retention can be calculated. Then two restriction time calculations were compared: the first is based on the mean (or fast) retention function and the calculated dose rates, the second is based on the slow retention function and the calculated dose rates. The first situation corresponds to the case of a patient who would have been attributed their own retention function and the second one to the method prescribed here. The calculation was carried out for the case of early discharge (5 h) and late discharge (18 h and 24 h). The assumed dose rates, retention functions and an example of calculated restriction times are given in part 4 of supplementary material A. As expected, using a conservative retention function resulted in conservative restriction time. In table 5 the excess days of restriction time are reported for our predefined scenarios (table 1), three discharge times and the cases of mean and fast excretion. If a patient has a mean excretion, using the conservative retention function but the correct dose rates results in an excess restriction time of at worst 3 d. If the discharge is early for five of seven scenarios the restriction time is in excess of 2 or 3 d. If the discharge is at 24 h, five scenarios give a maximum excess of 1 d. If a patient has a fast excretion, using the conservative retention function but the correct dose rates results in an excess of restriction time of at worst 8 d (early discharge, scenario C, contact with a child younger than 2 years). If the discharge is early for five of seven scenarios the restriction time is in excess of 3–8 d. If the discharge is at 24 h, for four scenarios the restriction time is in excess of 1–5 d.

3.5. Further remarks

In this study, the radiopharmaceuticals most frequently used in therapy were tentatively included: the choice was dictated by the current common use of iodine for different therapies and the expected increased use of others such as ^{177}Lu and ^{166}Ho . The case of ^{90}Y and ^{166}Ho , as microspheres was included for completeness since biokinetics is not an issue. Typical treatments with ^{90}Y microspheres lead to a dose rate of around $2 \mu\text{Sv h}^{-1}$ at 1 m after injection (Cournane *et al* 2019, Aberle *et al* 2020) and should not induce public dose of concern. However it has been reported in one study that the dose rate of a patient injected with ^{166}Ho

Table 5. Excess restriction time due to the conservative retention function (slow excretion) of ^{177}Lu -DOTATATE. Restriction time have been calculated for mean and fast excretion and compared with those obtained with the slow retention case.

Scenario	$t_{\text{out}} = 5 \text{ h}$		$t_{\text{out}} = 18 \text{ h}$		$t_{\text{out}} = 24 \text{ h}$	
	Excess restriction time (d) mean excretion	Excess restriction time (d) fast excretion	Excess restriction time (d) mean excretion	Excess restriction time (d) fast excretion	Excess restriction time (d) mean excretion	Excess restriction time (d) fast excretion
A	1	1	0	0	0	0
B	2	4	1	2	1	1
C	3	8	1	4	1	5
D	2	6	1	3	1	2
E	3	4	0	2	1	2
F	0	0	0	0	0	0
G	2	3	1	0	1	0

microspheres can be of the order of $40 \mu\text{Sv h}^{-1}$, 6 h after injection (Prince *et al* 2014). Whatever, for either ^{90}Y or ^{166}Ho microsphere therapies, if contact restriction time had to be calculated, evidence that the most suitable scaling function is the line source model has been presented.

The choice of recommended retention function suffers from some limitations. Our recommendation for ^{131}I -mIBG treatment is based on data for children and young adults and might not be suitable for adults. However, ^{131}I -mIBG is often used for treatments of neuroblastoma that are almost exclusively found in infants and young children (Carrasquillo and Chen 2016). For ^{177}Lu -PSMA it was not possible to give a conservative specific retention function and the one for ^{177}Lu -DOTATATE had to be used. This choice might not be as conservative as for the other radiopharmaceuticals since the data shown in Kurt *et al* (2018) and Mair *et al* (2018) indicate that in the case of ^{177}Lu -PSMA the variability among patients in retention is higher than for ^{177}Lu -DOTATATE. It even seems that the early retention of ^{177}Lu -PSMA is higher than that of ^{177}Lu -DOTATATE (Mair *et al* 2018). The choice of the retention function of ^{177}Lu -DOTATATE it is based on an extreme case but on a few patient data; it has been reported that the long-time retention might be higher than deduced from measurements in the first week, especially if several therapy cycles are taken into account (Gleisner *et al* 2015).

Another limitation is that the dose rate measurement is assumed to be carried out at the discharge date. The method and equation (7) could be modified to allow a different measurement time but it would certainly not induce a large difference in the calculation result.

A Monte Carlo computational approach might be useful to improve the accuracy of contact restriction time, biokinetics can be simulated (Lamart *et al* 2009, Chen *et al* 2016) and the dose received by caregivers and relatives computed taking into account their posture or ages (Han *et al* 2013, Geng *et al* 2015, Phuong Thao *et al* 2020). In particular, with such computations it could be computed if the dose rate scaling function depends on the time after administration. However, the accuracy of these computations would not be greater than the accuracy of the biokinetic models subtending them.

The assessment of contact restriction time should fulfil two opposite requirements: be conservative to comply with an appropriate dose constraint and be patient specific to avoid unnecessary constraint to patients and their relatives. Here it has been suggested to use a conservative retention function to fulfil the first requirement and to use individual measurements to compensate for the choice of the retention function. As illustrated above, taking into account the patient dose rate indeed compensates for the conservative choice of the retention function in some cases, but for some exposure scenarios the over-estimate can still be several days. In all cases it is recommended not to use the point source approximation since it is a clear cause of overestimation. If the patient's whole-body retention could be classified, even in a rough category, the assessment of restriction time would be less conservative. However, this would require several measurements of the dose rate, sufficiently extended in time, which is not necessarily feasible in the clinical routine. One option might be to take advantage of the whole-body retention deduced from the diagnostic agent when theranostic pairs are used, but this might be a lot of effort for a small improvement.

The calculation sheet that has been developed is a tool for the professional, explaining the radiation protection issues; delivering instructions to the patient is another issue. One might imagine that instruction templates could be prepared and that the results of the calculation sheet are pasted on this template. The calculation sheet only takes into account the exposure from the radiation emitted by patients, it should be kept in mind that patients should also be given instructions regarding the risk of contamination from excreta. The choice of dose constraints is also an issue. When several therapy cycles are scheduled it might be necessary to decrease the dose constraint per cycle to guarantee that a dose constraint for the whole

treatment is not exceeded. Such an approach would lead to relatively long restriction times and could be restricted to particular exposure scenarios, for example contact with young children. On the contrary, in some circumstances the dose constraint could be increased. Contact restriction times are set up to limit the exposure and hence reduce the risk of cancer induction; if the partner is relatively old (in Carlier *et al* (2004) 60 years was suggested) the risk is slightly reduced (ICRP 2007).

The scenarios and dose constraints given in the spreadsheet, or in other studies, are not prescriptive. The spreadsheet enables us to define scenarios and dose constraints as demanded by national authorities or professional bodies.

4. Conclusion

After nuclear medicine therapy patients should be released with written instructions to limit the exposure of their relatives and members of the public. It is illusory to think that purely patient-specific instructions could be delivered and a conservative approach, guaranteeing the radiation protection of the public, seems unavoidable. However, to avoid unnecessary worries and constraint to patients a degree of personalisation can be implemented thanks to dose rate measurements. The method and tool that have been developed in this work try to fulfil these opposite requirements and their advantages and limitations have been illustrated. The provided spreadsheet should be helpful and easy to use in clinical practice and can be freely adapted to accommodate specific needs.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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