Workshop on Standards and Measurements for Alpha Emitting Nuclides in Therapeutic Nuclear Medicine
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Measurement problems encountered in TAT clinical Practice: Radiation Safety

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Workflow

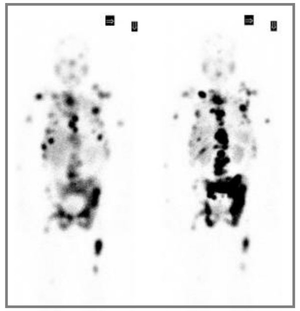
Admissions at the hospital — t_0

Radiopharmcaeutical administration — t_1

Imaging — t_2

Exsposure rate measurement — t_3

Patient discharge — t_4

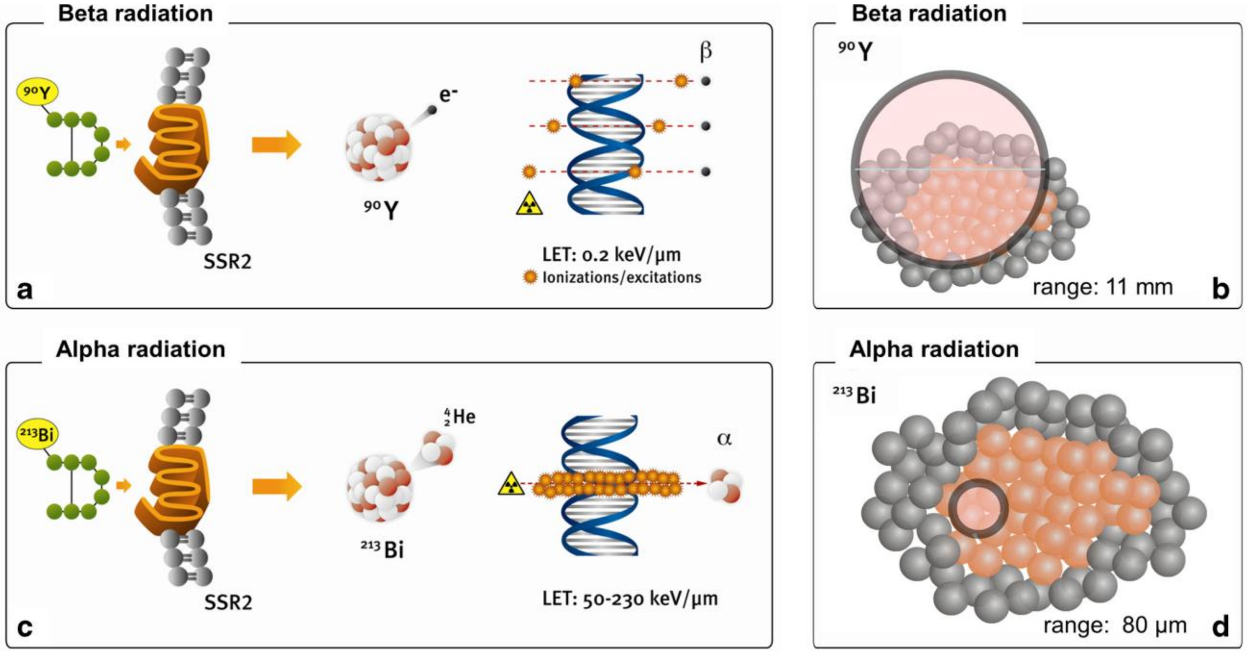


ANT POST

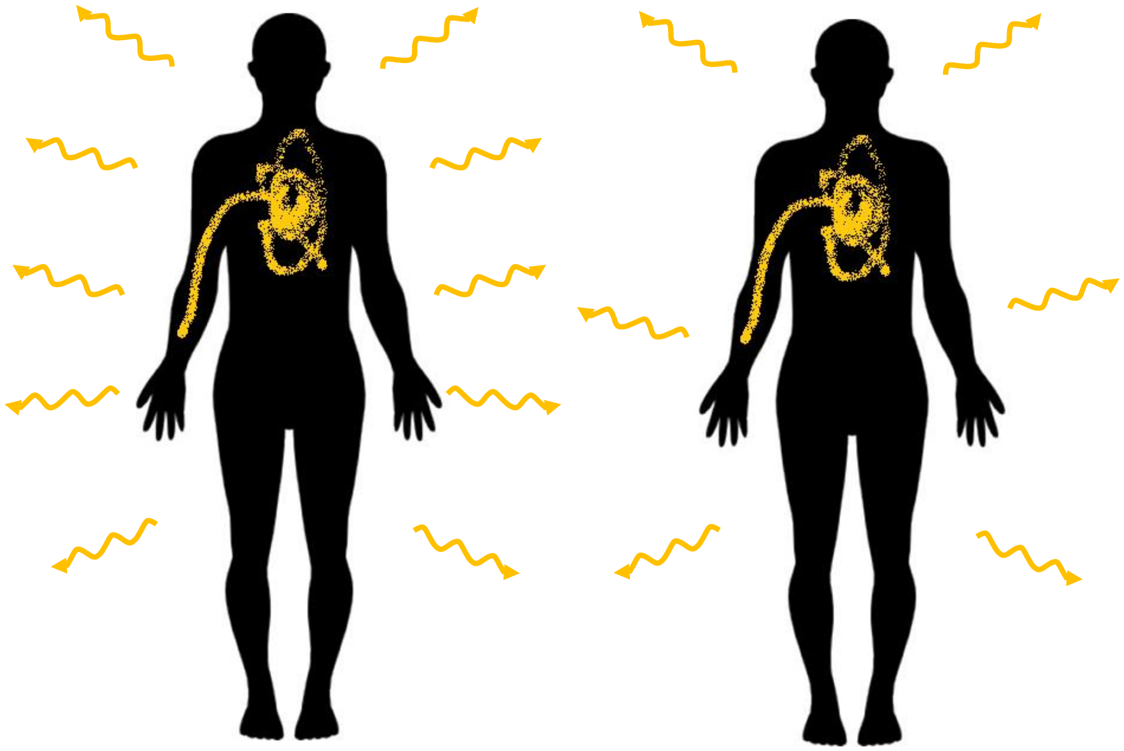
- ✓ Medical staff
- ✓ Technologists
- ✓ Radiopharmacists

- ✓ Family
- ✓ General public
- ✓ Enviroment

At cell level and at patient level



β + γ emitters (Lu-177) **α emitters**



- ✓ High LET
- ✓ High energy per decay

→

- ✓ Lower activity
- ✓ Lower exposure

α TRT vs β TRT

	Radionuclide	Half-life	# particles	E_{max} (MeV)	Total decay chian α energy (MeV)
α TRT	Th-227	18.68 d	5	7.61 (0.3%)	32.7
	Ac-225	10.0 d	4	8.4 (97%)	27.5
	Ra-223	11.43 d	4	7.61 (0.3%)	28.2
	Bi-213	45.59 m	1	8.4 (97%)	8.3
	Pb-212	10.64 h	1	8.8 (64%)	7.8
	At-211	7.12 h	1	7.4 (52%)	5.04
	Tb-149	4.12 h	1	3.9 (17%)	3.9 (17%)
β TRT	Y-90	2.67 d	1	2.284 (100%)	-
	Lu-177	6.65 d	3	0.497 (79.4%)	-

Total emission energy per decay for α TRT is 2 orders of magnitude higher than for β TRT

European Regulatory framework

Euratom 2013/59

Art. 28: Licensing for

(a) the deliberate administration of radioactive substances to persons

Art. 29: Authorization procedure

1. In the case of licensing member states shall take into account the indicative list in Annex IX.

Annex IX

Indicative list of information for licence applications as referred to in Article 29

(a) Responsibilities and organizational arrangements for protection and safety.
(b) Staff competences. including information and training.
(c) Design features of the facility and of radiation sources.
(d) Anticipated occupational and public exposures in normal operation.
(e) Safety assessment of the activities and the facility in order to:
(i) identify ways in which potential exposures or accidental and unintended medical exposures could occur;
(ii) estimate. to the extent practicable. the probabilities and magnitude of potential exposures;
(iii) assess the quality and extent of protection and safety provisions. including engineering features. as well as administrative procedures;
(iv) define the operational limits and conditions of operation.
(f) Emergency procedures.
(g) Maintenance. testing. inspection and servicing so as to ensure that the radiation source and the facility continue to meet the design requirements. operational limits and conditions of operation throughout their lifetime.
(h) Management of radioactive waste and arrangements for the disposal of such waste. in accordance with applicable regulatory requirements.
(i) Management of disused sources.
(j) Quality assurance.

Clearance levels

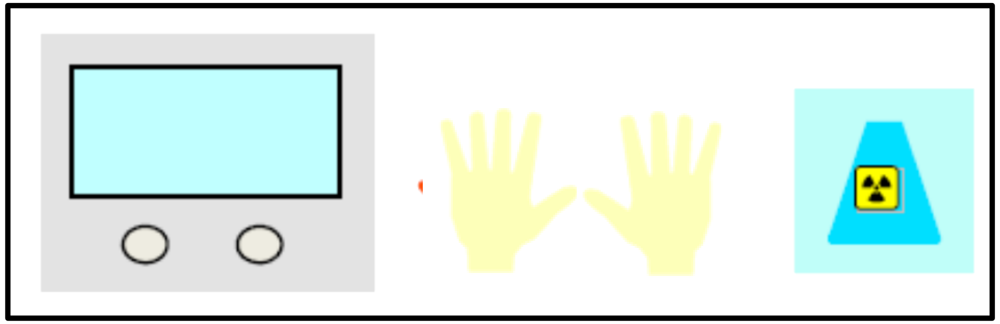
Regulatory limits

Criteria for facilities using radioactive substances	
Facilites required	✓ Rooms especially designed for the use of medical radionuclides ✓ Storage facilities ✓ Waste menagment facilities
Controlled areas	✓ Effective dose to the workers > 6 mSv ✓ Equivalent dose to the eye > 15 mSv ✓ Equivalent dose to the skin > 150 mSv → Category A Exposed workers
Uncrontrolled area	✓ ≤ 1mSv/year or 0.25 mSv/year for general public (NCRP 116)
Activity limitis for waste discarge	✓ Clearance levels ✓ The effective dose expected to be incurred by a member of the public due to the exempted practice is of the order of 10 µSv or less in a year.

- ✓ Alpha emitters may required to be shielded because of X rays and high energy gamma components (IAEA 2018)
- ✓ Ra-223 does not need high atomic number shield because the gamma rays do not contribute significantly to the dose

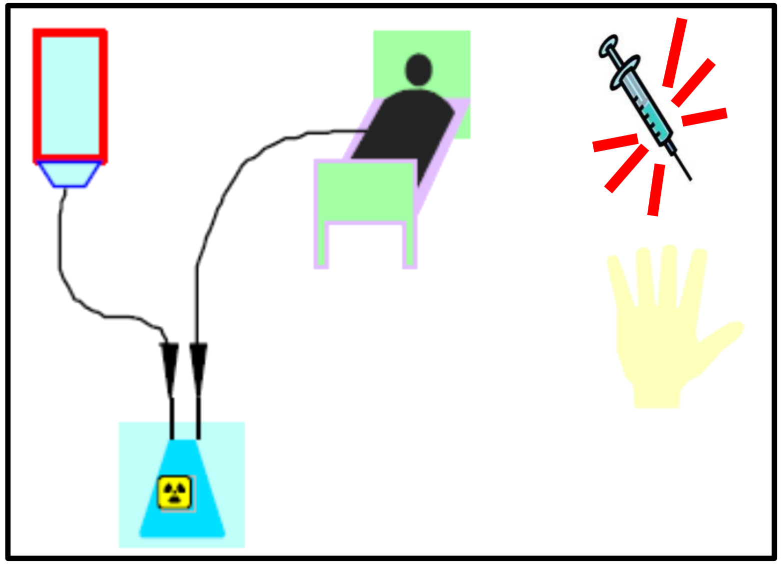
Radiation protection equipment

PREPARATION



- ✓ Isolator or hot cell with glove box
- ✓ Automated labelling system
- ✓ Filtretion of exhaust air duct
- ✓ Protective tablecloths
- ✓ Plexiglass + Pb shield for β and high energy γ
- ✓ Long handled tools
- ✓ Double gloves
- ✓ Single use equipment

INJECTION/INFUSION



- ✓ Plexiglas + Pb shield for β and high energy γ
- ✓ Double gloves
- ✓ Absorbent pad around the injection or infusion site

Infusion methods

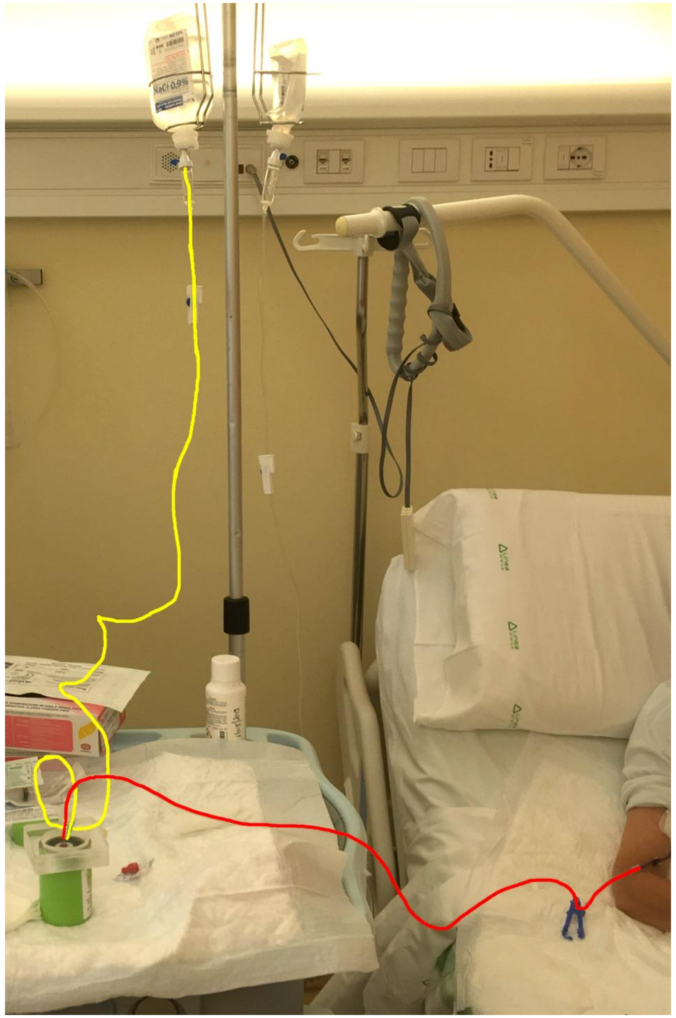
Slow bolus: ~ 1-2 m

- ✓ Ra-223
- ✓ Th-227
- ✓ Ac-225

Slow infusion: ~ 15- 30 m

Gravity method: without pump

With pump



- ✓ Ac-225

Dose conversion coefficients

	Point source	Vial 10 ml		Syringe 5 ml	Skin Contamination	
	$H_p(10)$ @30 cm (μSv/h/Bq)	$H_p(10)$@100 cm (μSv/h/Bq)	$H_p(0.07)$@ contact (μSv/h/Bq)	Hp(0.07)@contact (μSv/h/Bq)	Uniform deposit (μSv/h/(Bq cm^2))	0.05 ml droplet (μSv/h/Bq)
Th-227	1.70E-06	1.40E-07	6.40E-04	6.10E-02	8.10E+00	6.00E+00
Ac-225	4.40E-07	3.80E-08	1.80E-04	1.10E-02	3.50E+00	2.00E+00
Ra-223	5.80E-07	5.30E-08	2.40E-04	2.50E-02	3.40E+00	2.60E+00
Bi-213	3.40E-07	3.00-E08	1.40E-04	1.20E-02	5.20E+00	2.90E+00
Pb-212	2.50E-07	2.20-E07	1.20E-03	4.50E00	4.50E+00	1.80E+00
At-211	1.11E-07*	---	---	3.10E-06**	---	---
Tb-149	2.37E-06*	---	---	6.40E-06**	---	---

- ✓ Data from D. Delacroux et al *Guide pratique: Radionucleides & Radioprotection*, 2022
- ✓ 30 cm is the mean distance of the forearm
- ✓ 1 g cm^2 @ 100 cm in air that corresponds to the mean work distance
- ✓ 7 mg cm c^-2 in contact with the vial/syringe, at level of solution. The value corresponds to the maximum one
- ✓ *, ** values from *Radiation Protection Dosimetry 168 (1). 2016*
- ✓ **** $H_p(0.07)$@10 cm

Clinical application and exposure pathways

Radionuclide	Injected activity	Administration	Exposure pathway
Th-227	1.5 MBq – 6.1 MBq	✓IV injection	✓External (handling vials. syringe. waste) ✓Inhalation (Rn-219. airborn nuclides) ✓Ingestion (accident)
Ac-225	100 kBq/kg 0.06-0.07 MBq/kg (≈4-8 MBq)	✓IV injection ✓Slow infusion	✓External (handling vials. syringe. waste) ✓Ingestion/Inhalation (accident)
Ra-223	50 kBq/kg (≈ 3.5 MBq)	✓IV injection	✓External (handling vials. syringe. waste ✓Inhalation (Rn-219. airborn nuclides) ✓Ingestion (accident)
Bi-213	266-362 MBq 1-10.5 GBq 366-821 MBq	✓Intraarterial infusion ✓Systemic infusion ✓Intravesically	✓External (handling vials. syringe. waste) ✓Ingestion/Inhalation (accident)
Pb-212	7.4-27.4 MBq/m^2 (≈13.5- 50 MBq)	✓Intraperitoneal ✓IV injection	✓External (handling vials. syringe. waste) ✓Ingestion/Inhalation (accident)
At-211	71-347 MBq 34-355 MBq	✓surgically created resection cavity ✓Intraperitoneal	✓External (handling vials. syringe. waste) ✓Inhalation (during labelling) ✓Ingestion (accident)
Tb-149	5.5 MBq (preclinical) 5000 MBq (human)	✓**IV injection**	✓External (handling vials. syringe. waste) ✓Ingestion/Inhalation (accident)

Measured vs Teorethical Exposure

Radiosotope	Geometry	Distance	Measured Dose Rate (µSv/h/Bq)	H_p (µSv/h/Bq)
Ra-223	unshielded vial	Contact *	3.60E-05	2.40E-04
		Contact °	<1.00E-04	2.40E-04
		@10 cm °	<5.00E-06	5.30E-06
		@1m °	< 1E-07	5.30E-08
	unshielded syringe	Contact *	2.88E-04	2.50E-02
		Contact +	1.30E-02< Hp(0.07)<2.70E-02	2.50E-02

The measured values are generally lower than the theoretical ones

*Dauer LT et al *Health Phys* 2014

° Hosono M et al *Ann Nucl Med* 2019

+ El Mantani Ordoulidis Set al *Radiat Prot Dosimetry* 2018

Clinical scenario

External exposure to Tecnologists and/or Medical staff

PREPARATION & INJECTION

Phase description	Professional staff	Time (s)	Shielding
Preparation of a single dose	Technologist	✓ 120 @ contact with vial ✓ 300 @ 30 cm from the vial	The vial is in a lead holder
Injection of a single dose	Medical staff	✓ 120 @ contact with syringe ✓ 120 @ 5 cm from the syringe (as an alternative evaluation) ✓ 300 @ 30 cm from the syringe	Beta-gamma shielding is reccomended to adhere the ALARA principles
Patient care (interacting with patient)	Medical staff/nurse	✓ 600 @ 50 cm	No shield

	Single procedure	Preparation 		Administration 			Patient care
	Activity (MBq)	E @contact (µSv)	E @ 30 cm (µSv)	E @ contact (µSv)	E @ 5 cm (µSv)	E @ 30 cm (µSv)	E @ 50 cm (µSv)
Th-227	6	1.28E+02	7.78E-01	1.22E+04	2.16E+00	8.50E-01	6.12E-01
Ac-225	8	4.80E+01	2.81E-01	2.93E+03	2.56E+00	2.93E-01	2.11E-01
Ra-223	6/3.5	4.80E+01	2.94E-01	2.92E+03	2.29E+00	1.69E-01	1.22E-01
Bi-213	316	1.40E+03	8.33E+00	1.15E+05	4.22E+01	8.50E+00	6.12E+00
Pb-212	50	2.00E+03	1.02E+01	7.50E+06	2.80E+01	1.04E+01	7.50E+00
At-211	350	1.45E+02	3.24E+00	---	1.24E+02	3.24E+00	2.33E+00
Tb-149	5000	4.27E+03	9.86E+02	---	4.27E+03	9.86E+02	7.10E+02

- ✓ *Data in agreement with the Aro et al *J Med Imaging Radiat Sci 2019*
- ✓ The shallow dose at contact is estimated in correspondence of arrow position and is the maximum one;
- ✓ To consider the distance between the radiopharmaceutical and the fingers, the Hp(0.07) from Otto *(Rad. Prot. Dos 216)* is considered
- ✓ In case of systemic infusion by means a pump, the dose contribution is given by the dose in contact with the vial reported in column 2

		Measured	Estimated
Bi-213*	Effective dose to the radiopharmacists	5.42 µSv 316 MBq; procedure of ~35 ~min	
	Equivalent dose to the radiopharacists extremities	10.2 µSv 316 MBq; procedure of ~35min	
	Effective dose to the injectors	0.33 µSv 288 MBq; procedure of ~3.25 min	0.48 µSv
	Equivalent dose to the injectors extremities	1.45 µSv 288 MBq; procedure of ~3.25 min	42 µSv
	Dose rate from patients	7.15E-09 µSv/h/MBq @ 1 m just p.i 9.13E-08 µSv/h/MBq @ 0.1 m just p.i 0.22 µSv/h @ 1 m 4 h p.i	3E-08 µSv/h/MBq @ 1 m just p.i 3E-06 µSv/h/MBq @ 0.1 m just p.i 0.24 µSv/h @1 m 4 h p.i
Ra-223+	Dose rate from patients	<2 µSv/h/MBq @ contact just p.i 0.11 µSv/h/MBq @ 30 cm just p.i 0.02 µSv/h/MBq @1 m justp.i	21 µSv/h/MBq @ contact just p.i 0.6 µSv/h/MBq @ 30 cm just p.i 0.05 µSv/h/MBq @ 1 m just p.i
Ac-225°	Dose rate from patients	1.7 µSv/h 4.8 MBq @ contact 0.3 µSv/h 4.8 MBq @ 1 m	76 µSv/h 4.8 MBq @ contact 0.2 µSv/h 4.8 MBq @ 1 m

*Thakral P et al *J Nucl Med Technol* 2020
+ Dauer LT et al *Health Physics* 2014
° Craig AJ et al *Quart J Nuclear Med Molec Imaging* 2023

Internal exposure

The assessment of doses to workers routinely or potentially exposed to radiation through intakes of radioactive material constitutes an integral part of any radiation protection programme helping to ensure acceptably safe and satisfactory radiological conditions in the workplace.

Pathways of intake

- Inhalation → main contamination route (ICRP 54 and ICRP 78)
- Ingestion

RELEASE OF RADIOACTIVITY

- ✓ Evaporation during labelling (heating, pressurizing. etc..)
- ✓ Re-suspension of radiocativity from contaminated surface due to a spill of radionuclide
- ✓ Radioactive in exhaled breath from patients
- ✓ Indirect contamination via patient escretion or waste

Committed effective dose

$$E = h_{inh} \times I$$

$$I = v \times C \times t$$

E: Committed effective dose
h_{inh}: dose conversion factor [Sv/Bq]
I: intake [Bq]
r: ventilation rate [$m^3\ h^{-1}$]
C: Activity concentration [Bq m^{-3}]
t: procedure duration [h]

Ventilation rates (ICRP 66)

Activity	**Ventilation rates [$m^3\ h^{-1}$]**
Sleep	0.45
Rest-Sitting	0.54
Light excercise	1.5
Heavy excercise	3.0

$$C = \frac{A \times F}{V \times n \times O}$$

A: Activity [Bq]
F: dispersal factor
V: room volume [m^3]
n: air exchanges per hour [h^{-1}]
O: Occupancy factor [h/day]

Discarged air indoors

✓ C can be estimated by using some nominal parametres or can be measured by an air pump system

Committed effective dose estimation

Scenario Parameters

Dispersal rate	0.001
Ventilation rate [m^3/h]	1.2
Room volume [m^3]	36.5
Air exchanges per hour [h^{-1}]	10
Occupancy factor [h/day]	8
Work time t [h]	0.5

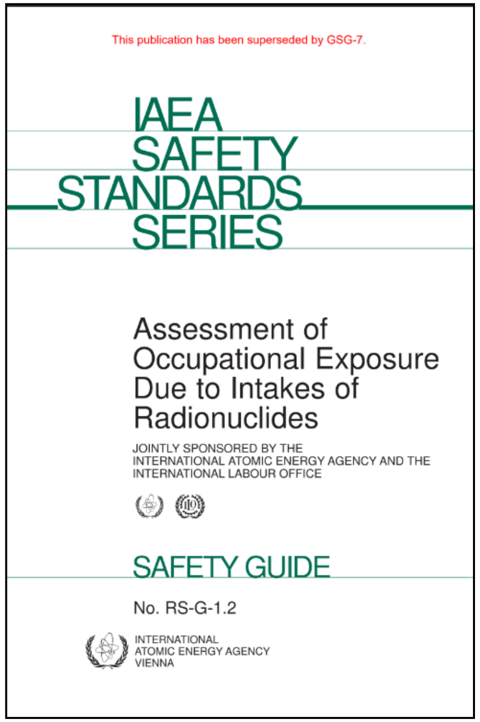
Administration/injection

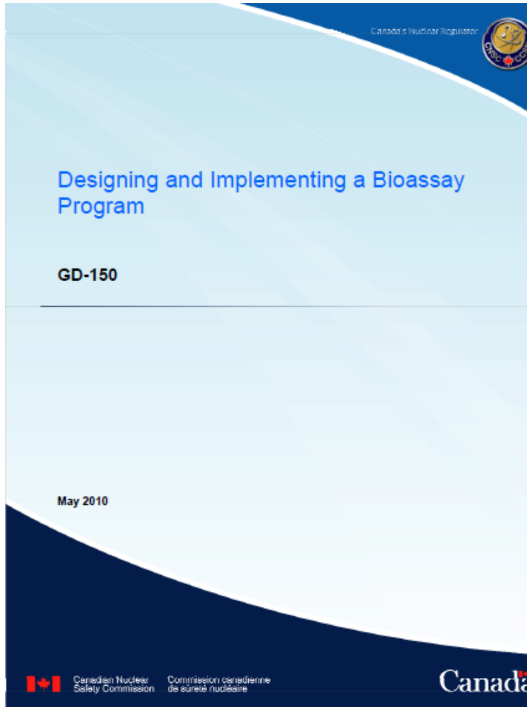
	h_{inh} (Sv/Bq)	AMAD & clearance	Activity (MBq)	Committed Effective dose (μSv)
Th-227	9.60E-06	1 μ. S	6	1.18E+01
Ac-225	7.90E-06	1 μ. S	8	1.30E+01
Ra-223	6.90E-06	1 μ. M	6	8.51E+00
Bi-213	4.10E-08	5 μ. M	316	2.53E+00
Pb-212*	5.00E-08	5 μ. M	50	5.14E-01
At-211**	1.10E-07	5 μ. M	350	7.91E+00
Tb-149**	4.30E-09	1 μ. M	5000	4.42E+00

- ✓ Values from Delacroix et al *Radionuclides et Radioprotection. Guide Pratique (2022)*
- ✓ **Values from ICRP 119
- ✓ * For Pb-212 the values reported in Delacroix et al is more cautelative
- ✓ The maximum value is ≈ 10 μSv

Internal contamination risk assessment

- ✓ IAEA. Safety Guide RS-G-1.2, 1999 (Appendix I)
  - ✓ Norma ISO 16637 (2016)
- ✓ Canadian Nuclear Safety Commission, Guidance Document GD-150, 2010





These documents provide quantitative approach for identification of workers, determination of the need for monitoring, and selection of a suitable monitoring programme

Designing and Implementing a Bioassay Program GD-150

- ✓ Dose assessment should be performed for all workers who have a reasonable probability of receiving a committed effective dose ≥ 1 mSv/year
- ✓ If the committed effective dose is ≤ 1 mSv/year, the dose may be estimated using workplace monitoring

Potential **I**ntake **F**actor **(PIF)**

$PIF = 10^{-6} \times R \times C \times D \times O \times S$

- ✓ 10^{-6} il fattore di Brodsky
- ✓ R: release factor
- ✓ C: confinement factor
- ✓ D: dispersibility factor
- ✓ O: occupancy factor
- ✓ S: special form factor

FACTORS INVOLVED

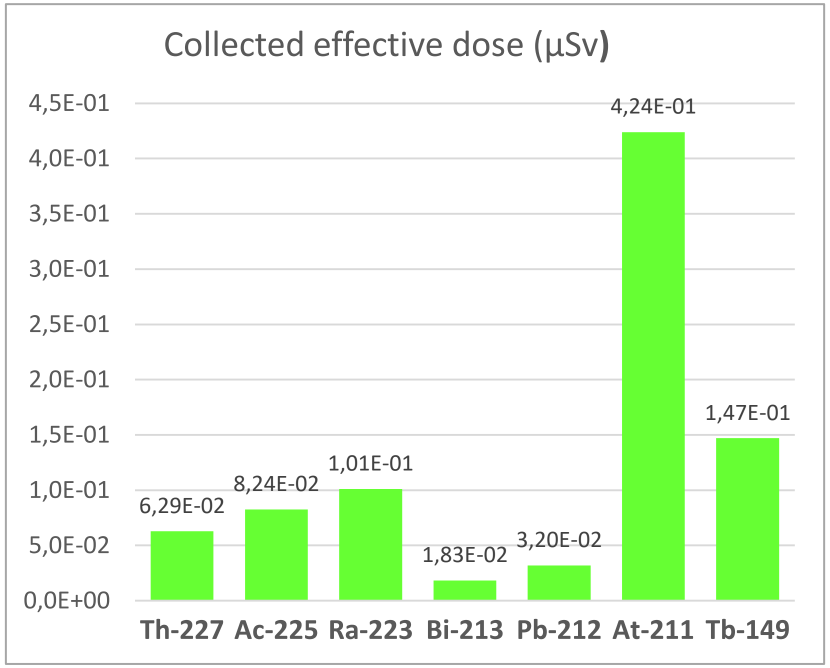
- ✓ Amount of handled activity
- ✓ Radionuclides
- ✓ Chemical and physical characteristics
- ✓ Type of containment used
- ✓ Nature of operations performed

Partecipation in a bioassay programm

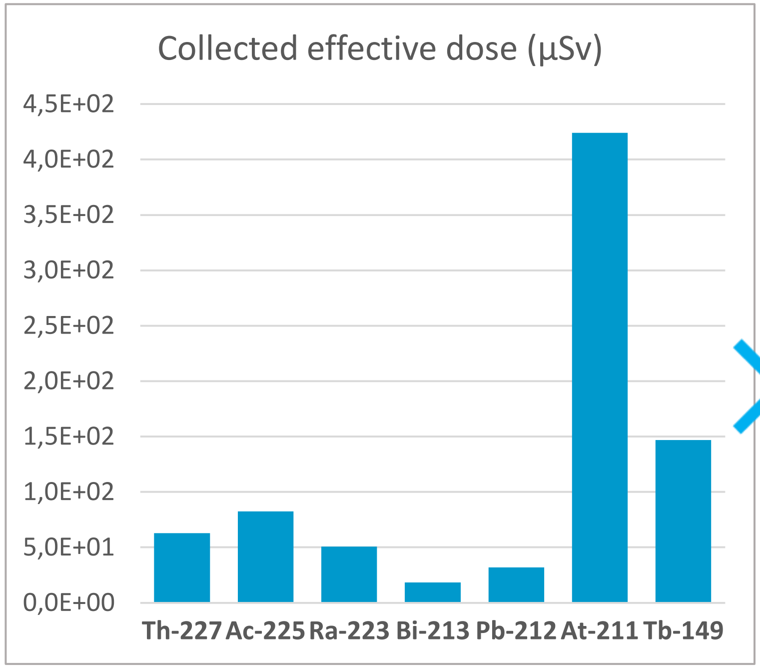
Radio-nuclide	Activity (MBq)
Th-227	6
Ac-225	8
Ra-223	6
Bi-213	300
Pb-212	50
At-211	350
Tb-149	5000

R = 0.01; C= 0.1 / 100

Preparation/injection



Contamination

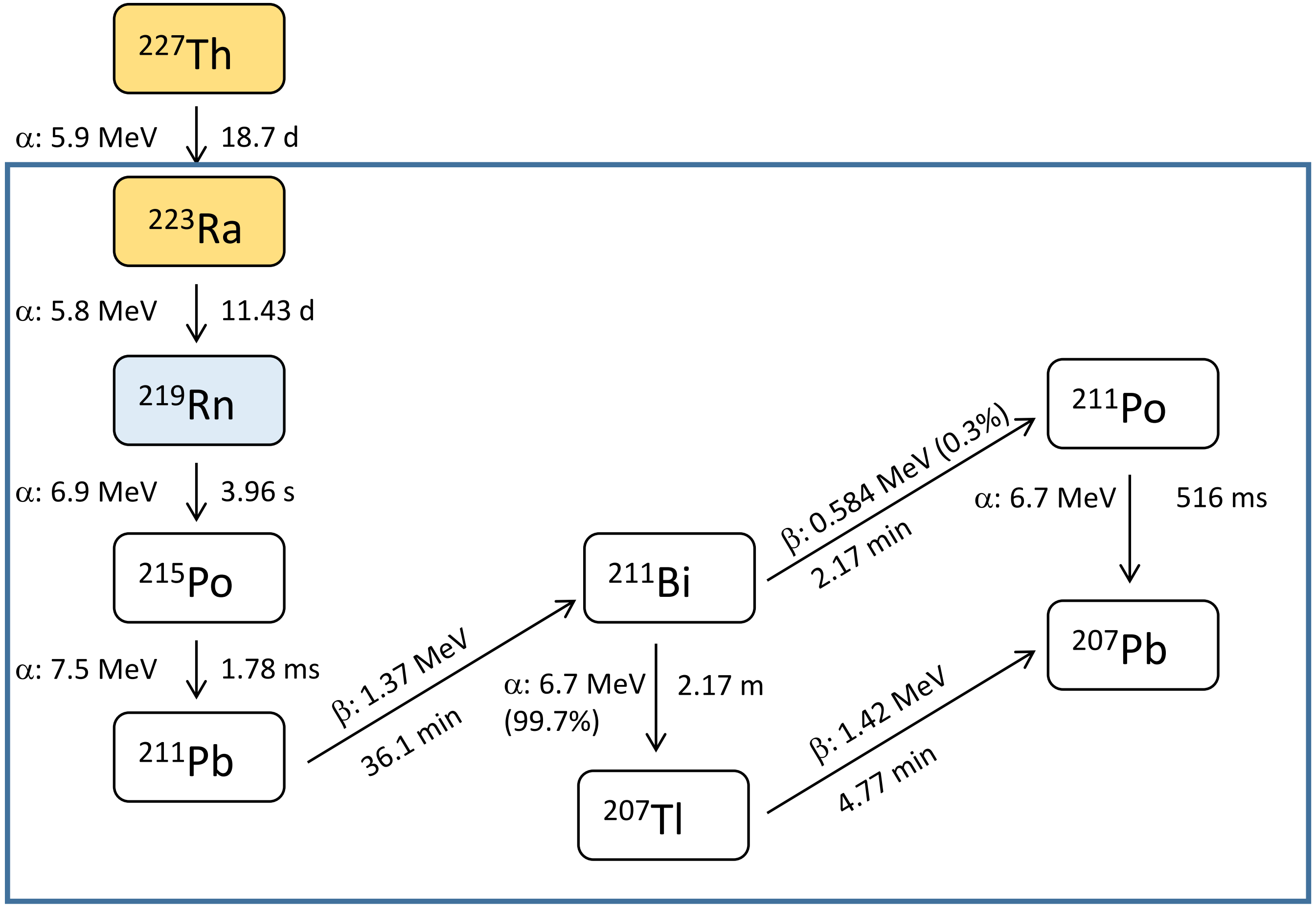


$\times N_{\text{procedures}}$

R= 0.01 ➡ liquid
C=0.1 ➡ enhanced fume hood
C=100 ➡ surface contamination in a room with normal ventilation

- ✓ The criterion for the bioassay partecipation is 1 mSv
- ✓ **Fecal bioassay is preferred** since feces contain a larger % of activity than other escreta

Rn-219 Inhalation risk

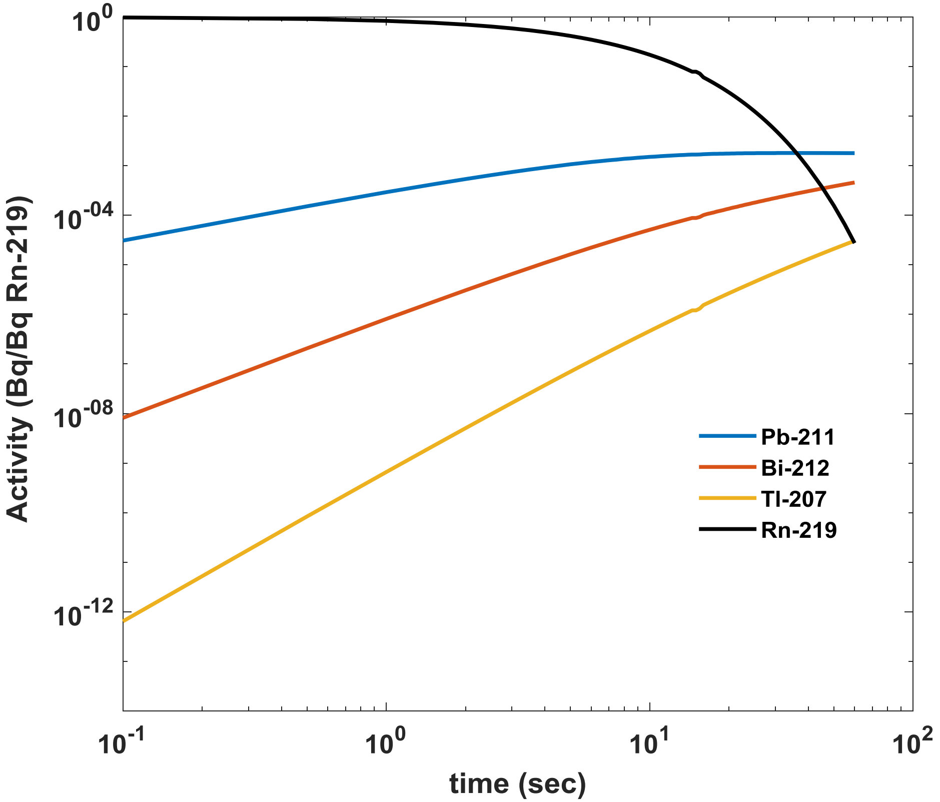


The Rn-219 inhalation risk is common to Th-227 and Ra-223

- ✓ Rn-219 has a very short half-life (4s) and is generally less able to escape from the point where it is formed (ICRP 137)
- ✓ Due to saturation, solubility and physical hal life considerations, the assumption of volatility is highly unlikely *(MG Stabin and A Siegel Health Physics 2015)*

Rn-219 does not likely represent an inhalation risk and the exposures to Rn-219 and its progeny in the workplace are generally low and can be ignored.

Spilled radioactive: Rn-129 and daughters



	Rn-219	Po-215	Pb-211	Bi-211	Tl-207	Po-211
N (Bq-s/Bq)	5.57	5.57	2.57	2.36	1.84	0.00658
h_{inh} (Sv/Bq)	7.79E-11* 4.8E-11**	1.97E-13	3.46E-11* 6.6E-08**	1.76E-9* 4.8E-09**	8.04E-12	1.72E-11
Committed Effective dose (mSv)	2.70E-04 1.64E-04	6.73e-07	5.46e-05 1.04e-01	2.54E-03 6.93E-03	9.07e-06	6.94E-08
Total Committed Effective Dose (mSv)					2.9E-03* 1.1E-01 **	

In 60 s the Rn-219 (Po-215) activity drops to 10^{-5} of its initial activity, while its progeny activity increases

*MG Stabin and JA Siegel *Health Physics 2015*

**ICRP 137

Spilled radioactive: effective and equivalent dose

External exposure

$$E = t\,\pi\,\Gamma\,C_a\,ln\left(\frac{r^2+h^2}{h^2}\right)$$

Γ: gamma ray constant
C_a: activity concentration [Bq m^{-2}]
r: radius of teh source [m]
h: height above the source [m]
t: exposure time [h]

Skin contamination

Unifrom deposit ➡ Surface =100 cm^2

0.05 ml droplet ➡ Volume = 6 ml

Skin contamination

Radionuclide	Activity (MBq)	External exposure (mSv)	Uniform deposit (mSv)	0.05 ml droplet (mSv)
Th-227	6	1.76E-03	2.43E+02	1.50E+02
Ac-225	8	6.07E-04	1.40E+02	6.67E+01
Ra-223	6	3.50E-04	5.95E+01	3.79E+01
Bi-213	316	1.76E-02	7.80E+03	3.63E+03
Pb-212	50	2.15E-02	1.13E+03	3.75E+02
At-211	350	6.70E-03	---	---
Tb-149	5000	2.04E+00	---	---

- ✓ Estimation for Ra-223 are in agreement with data in MG Stabind and JA Siegel *Health Physics 2015*
- ✓ The scenario for skin dose estimation is extremely conservative; in a realistic scenario the dose would be an order of magnitude or more lower

Patient release

Euratom 2013/59 Art. 56 Optimization → Dose contraints for general public. carers and comforters

Model to estimate the dose

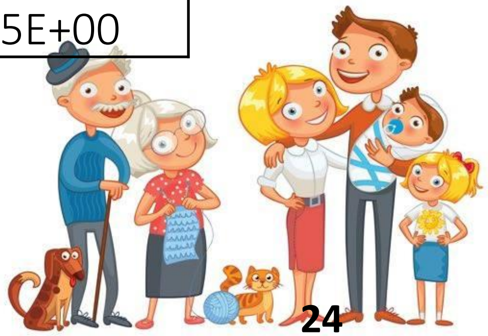
- ✓ The activity decreases according to the physical half-life
- ✓ $E = EF \times \int_{t_0}^{\infty} \dot{E}\, dt = EF \times \frac{A_{0 \times \Gamma}}{r^2 \times \lambda_{phys}}$
- ✓ EF= exposure factor: Family: 0.5; General public: 0.25

Effective dose E (µSv)

Radionuclide	Activity (MBq)	Family	General public
Th-227	6	5.16E-01	2.58E-01
Ac-225	8	9.52E-02	4.76E-02
Ra-223	3.5	3.62E+01	3.14E-02
Bi-213	316	9.20E-03	4.60E-03
Pb-212	50	1.50E-01	7.50E-02
At-211	350	3.12E-02	1.56E-02
Tb-149	5000	5.50E+00	2.75E+00

$\times N$ cycles/year

No restriction are required to limit contact with others but extrahygiene precautions



Reccomendations for patients

- ✓ **Sitting** while **urinating or defecating**; the water is to be flushed twice every use
- ✓ Promptly **cleaning** any vomitus or any **bodily fluids**, using disposal gloves
- ✓ **Wash hands** with soap and water after wiping up any spills, in case of contact with bodily fluids and after using the toilet
- ✓ In case of need of medical care, **informing the healthcare provider** of the previous treatment with an alpha-emitting radionuclide
- ✓ **Wash** the patient’s **clothes, towels and bed sheets** separately, using an extra rinse cycle, if possible

Last issue: waste menagment

Solid waste:

- ✓Any residual or materials used in connection with the preparation or administration
- ✓Solid waste should be stored until it reaches the levels of regulatory criteria

Clearance levels: Table A. Part 1. Annex VII Euratom 95/2013

- ✓ For activity concentrations not compling with clearance levels, it is necessary to perform a radiological impact assessment in the light of general criteria

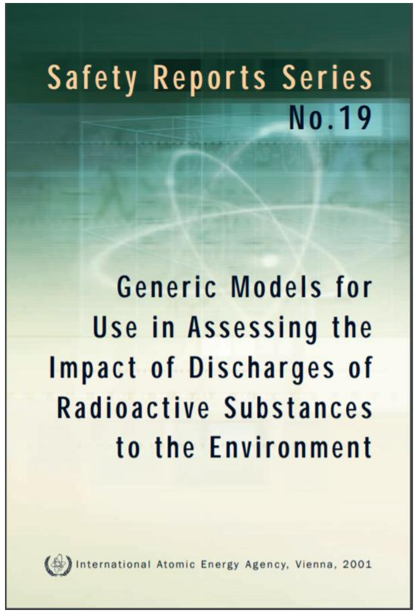
Patient escreta

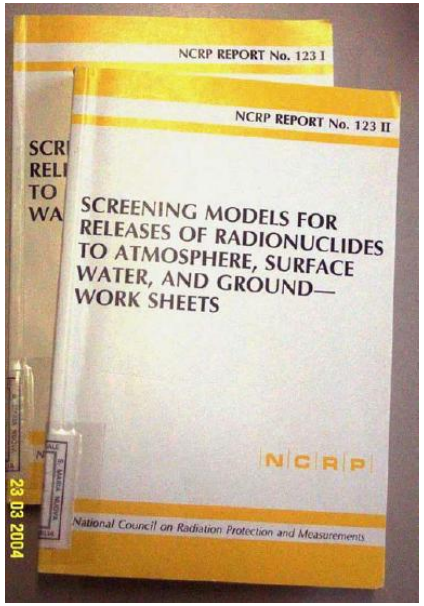
- ✓Can be disposed directly to the sewage system
- ✓Can be stored in dedicated tanks before the release in the sewage system (decay method)
- ✓ It is necesary to perform a radiological impact asssessment to assess the pathways of exposure and the dose to the cirtical groups

The effective dose to a member of public due to the practice should be of the order of 10 µSv or less in 1 year

Risk assessment to the enviroment

TFs for terrestrial foods					BF
	TF (vegetables)	TF (dry forage)	TF(milk) $(d \cdot L^{-1})$	TF (beef) $(d \cdot L^{-1})$	Freshwater Fish (L/kg)
Ac	0.001	0.1	$2 \cdot 10^{-6}$	$2 \cdot 10^{-5}$	15
At	0.2	0.9	0.01	0.01	15
Bi	0.1	0.5	**0.001**	0.002	15
Pb	0.004	0.1	$3 \cdot 10^{-4}$	$8 \cdot 10^{-4}$	**300**
Ra	0.04	0.2	0.001	0.001	50
Tb	0.002	0.1	$6 \cdot 10^{-5}$	0.002	25
Th	0.001	0.1	$5 \cdot 10^{-6}$	$1 \cdot 10^{-4}$	**100**
Tc	**5**	**40**	0.001	$1 \cdot 10^{-4}$	20
F	0.02	0.1	0.007	**0.02**	10
Lu	0.002	0.1	$6 \cdot 10^{-5}$	0.002	25





Transfer factors (TF) or bioaccumulaion factors (BF) are the fraction of activity that terrestrial food and freshwater fish abosrb from the soil and water, respectively

Discussion & conclusions

- ✓ α-emitters can be handled and administered safely thanks to:
  - **Protective equipment**
  - **Training**
  - **Procedures**
  - **Instrumentation**

- ✓ The main risk is due to the **skin contamination** but licensee's policies and procedures should minimize the associated dose (**double gloves, protective clothes…**)

- ✓ The patient can come back to his everyday life with **just reccomendations** to avoid internal cotamination of others individuals

Thanks!

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