

Use of a new isotope, ^{223}Ra

1. What is ^{223}Ra ?
2. Xofigo
3. Special hazards and risks
4. Implementation at the Erasmus Hospital
5. The issue of wastes
6. Incident(s)
7. Conclusions



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1. What is ^{223}Ra ?

- ^{223}Ra : one of the very numerous isotopes of Ra
- Half-life: 11.4 days
- Ca analogue → quickly localises in areas of growth of bone tissue
- Range of the α in air: ± 6 cm
- Range of the α in tissue: < 100 μm

α	95%	6 MeV
β	4%	± 1 MeV
γ	1%	81, 84, 154, 269 keV

$^{223}\text{RaCl}_2$ (radium dichloride – Xofigo)

- Calcium analogue: captured by the bone (44-77% 4h after I.V.)
- Primary means of elimination: digestive tract (faecal matter)

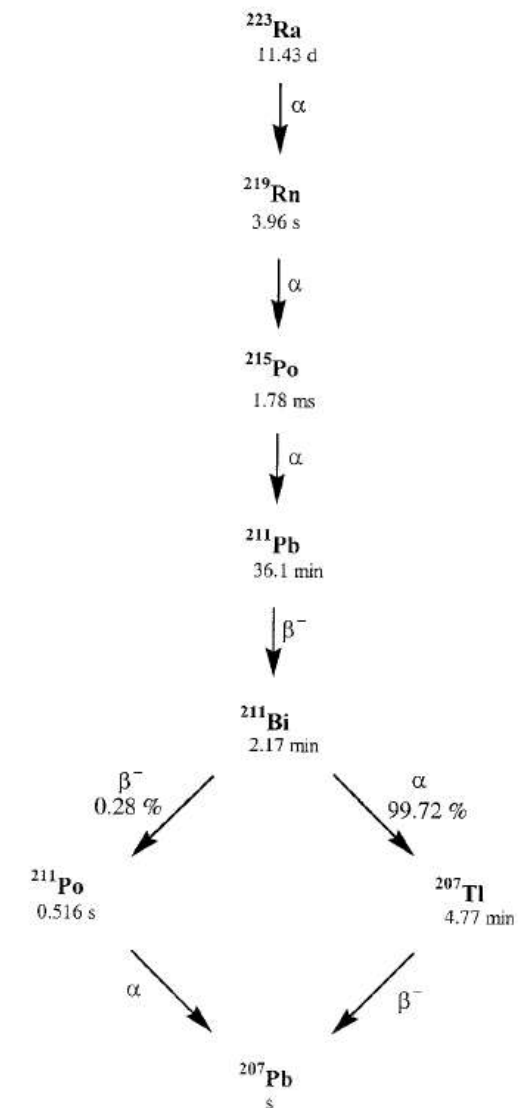
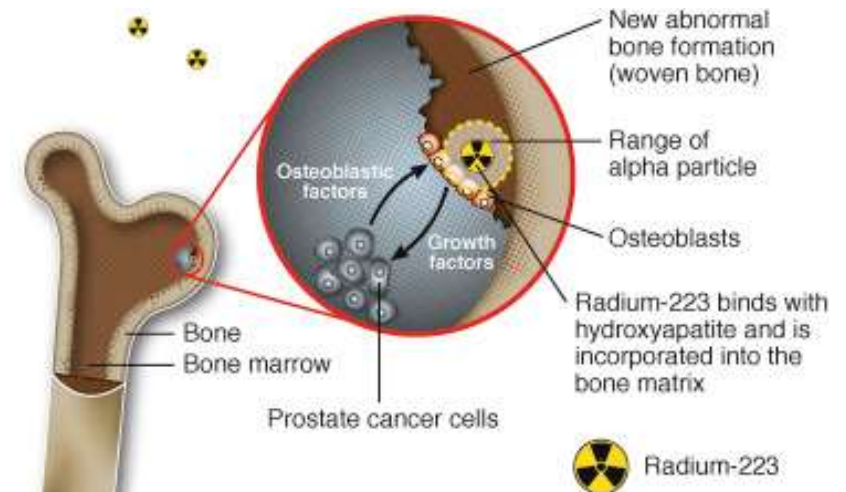
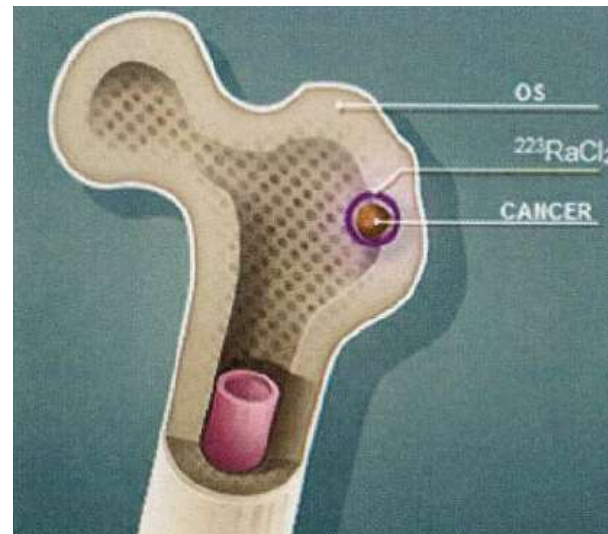


Fig. 1. Decay of ^{223}Ra .

2. Xofigo

XOFIGO is indicated for the treatment of patients with castration-resistant prostate cancer who have predominant symptomatic bone metastases.

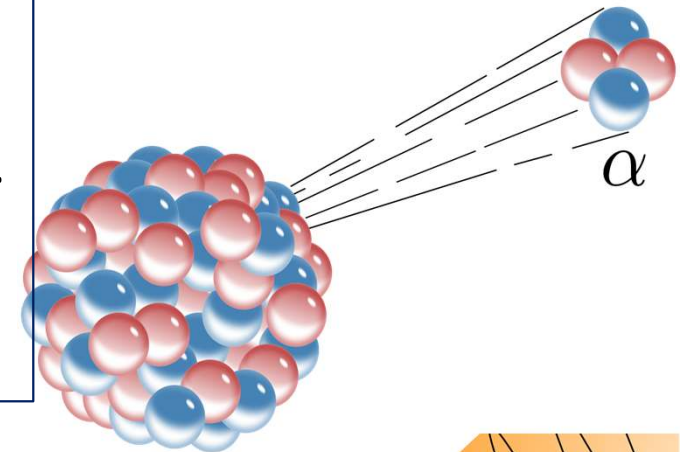


- Ready-to-use solution – Secure and easy to use – No vector agent
- Low injected activity: 55 kBq per kg or 3.85 MBq (104 μ Ci) for a 70 kg patient
- Packaged in a vial, standardised and stable
- 6 MBq (162 μ Ci) of ^{223}Ra per vial (day of calibration) - 10 ml vial including 6 ml of solution.
- Concentration of radioactivity = 1100 kBq/ml (day of calibration)
- Stability = 28 days

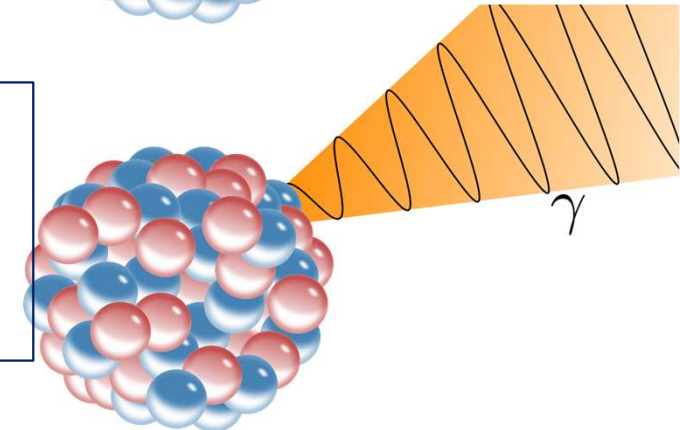
3. Hazards – Risks (1)

- ^{223}Ra : α and (β) γ emitter

- α : radiation emitted by unstable nuclei of high atomic mass. Composed of two protons and two neutrons.
Energy deposition per distance travelled: very high \rightarrow short range
 \rightarrow Risk: contamination
 \rightarrow Measurement and detection: difficult



- γ : electromagnetic radiation
Energy deposition per distance travelled: low \rightarrow long range
 \rightarrow Risk: irradiation +++ and contamination
 \rightarrow Measurement and detection: easy



The major risk to take into account: α contamination

3. Hazards – Risks (2)

Exposure of personnel

Dose rates ⁽¹⁾	Ra-223	Tc-99m
to the fingers on contact with the original vial	162 µCi (6 MBq): 1.44 mSv/h	800 mCi (30 GBq): 5920 mSv/h
on contact with a syringe	100 µCi (3.7 MBq): 92.5 mSv/h	20 mCi (740 MBq): 259 mSv/h

Dose rates and dose ⁽²⁾	Dose rate (µSv/h)	Effective dose for 30 treatments (inj) (µSv)
Receipt of the package (8MBq)	0.157	0.31
Patient injection and follow-up (5 MBq)	0.460	0.92
Management of wastes	0.070	0.07
TOTAL	-----	1.30

(1) According to Notified Body

(2) Feedback... Gustave Roussy – 06/2014

3. Hazards – Risks (3)

Contamination of personnel

Annual limit on intake (ALI): 200 kBq (5.4 μ Ci), and even less (100 kBq) if the decay products are taken into account

Committed dose⁽¹⁾:

- Contamination of a 0.05 ml drop during injection
- 70 kg patient → 3.85 MBq (104 μ Ci) in 3.5 ml
- Contamination = 50 kBq
- → Committed dose: \pm 130 mSv

(1) According to Notified Body

Excreta



Primary excreta via the urine (-) and faeces (+) during the first week → radioprotection measures if hospitalisation

3. Hazards – Risks (4)

Miscellaneous

1. Invasive examination → to be planned before injection of the ^{223}Ra .
2. Hospitalised patient or patient whose state of health involves a risk of quick hospitalisation afterward → the injection should ideally not be given.
3. Patient requires an urgent surgical procedure after the injection
 - Notify the RPE (RPO)
 - Inform the personnel of the risk of contamination (+ dosimetry)
 - Control of the wastes
4. Death of the patient ≤ 59 days: special precautions imposed by the FANC

4. Implementation (1)

 	Auteur principal: Boeckmans Sophie	ID: ERASME-18-1444
	Radio-isotopes-Radium-223 informations pour le patient	Version: 1.0
		Date d'application: 23/10/2019
		Fin de validité: 23/10/2022

1. Why a treatment with Xofigo?
2. What is Xofigo treatment?
3. The benefits of treatment with Xofigo
4. Tolerance of Xofigo
5. The steps of treatment
 - a) Before
 - b) During
 - c) After (including death)

4. Implementation (1)

- a) Receipt of the package: check of the compliance and integrity of the package and the Xofigo
- b) Storage: in a shielded cabinet
- c) Preparation:
 - Special work station: Biological Safety Cabinet (BSC) + shielding (plexiglass and Pb)
 - Lab coat
 - Double pair of gloves
 - Dosimeter
 - Contamination meter nearby
 - Special management of wastes (see below)
 - Syringe + BD PhaSeal Injector™ device (compatible with the Luera™ 100 µm)
 - Check for absence of contamination. If problem, call RPO.
- d) Administration:
 - Lab coat
 - Double pair of gloves
 - Dosimeter
 - Contamination meter nearby
 - Special management of wastes (see below)
 - Check for absence of contamination. If problem, call RPO.
 - Radiation physicist available

MPE and RPE involved but not necessarily present.
RPO present

4. Implementation (2)

BD PhaSeal™ system

Closed-system transfer device that mechanically prevents the passage of external contaminants into the system, as well as any external leak of hazardous substances in liquid or vapour form.



5. Wastes (1)

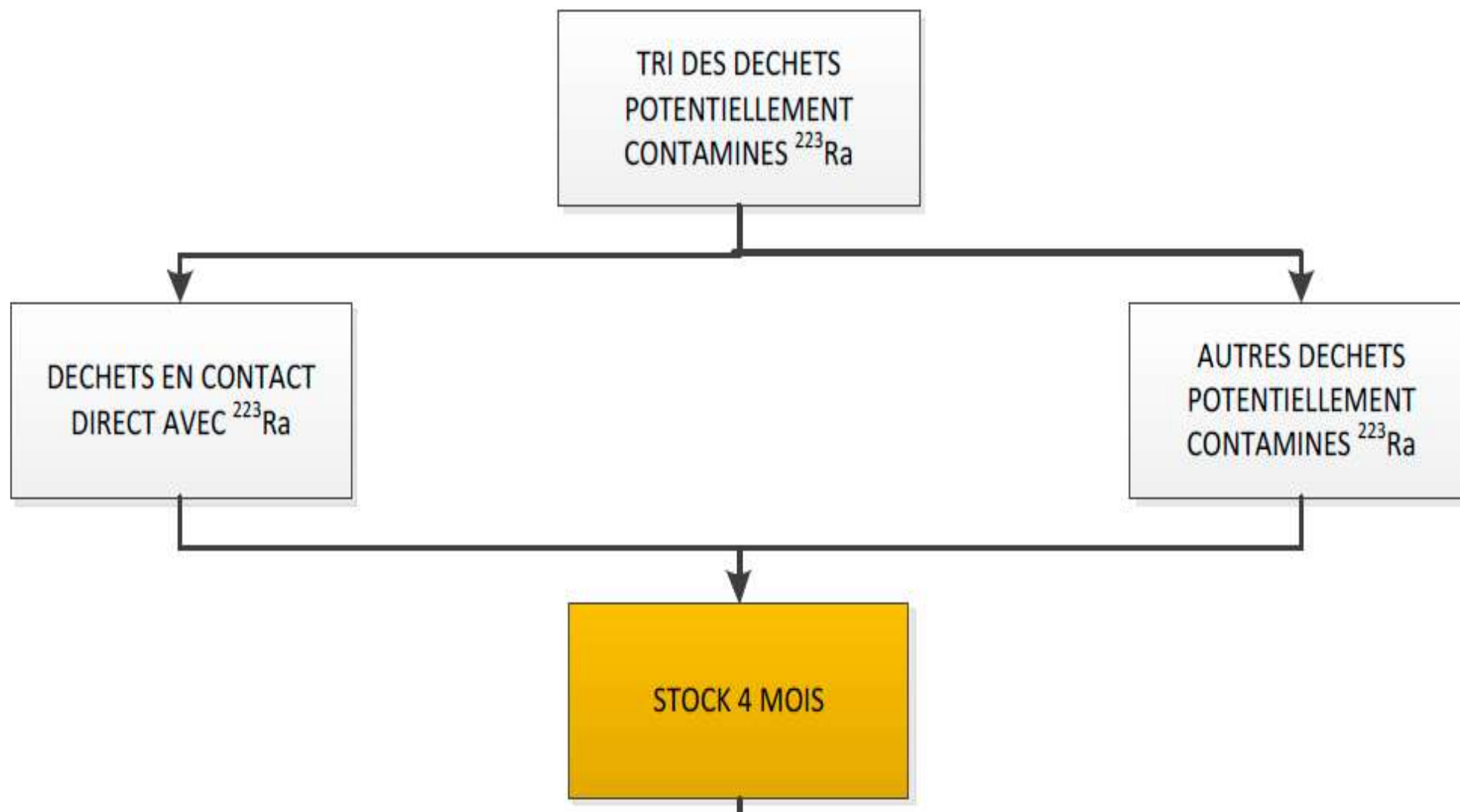
^{223}Ra ($T_{1/2}$: 11.43 days) is very often contaminated with ^{227}Ac ($T_{1/2}$: 21.77 years)

RGPRI [*General regulations for protection of the public, workers and the environment against the hazards of ionising radiation*] (Art 35.2): “If radioactive substances with a **lifespan of less than six months** are used, compliance with the conditions and levels of release... is not sufficient.

Disposal... of these substances can only take place after **almost complete decay**.

Storage of these substances for a period equivalent to at least ten half-lives is required... This storage will be extended for the period necessary to ensure almost complete decay.”

5. Wastes (2)



5. Wastes (3)

Bayer informs the Nuclear Medicine department and the SIPP-CP [*Internal Service for Prevention and Protection at Work – Prevention Councilor*] of the measured Ac-227 activity for each batch at 100 days post-production (limit of detection: 4.1 Bq/6ml)

The activity of the wastes will be calculated in any event (by the MPE, and validated by the RPE).

The activity of the wastes will be calculated on the basis of the remaining solution (X ml) x the specific activity given by Bayer (y Bq/ml):

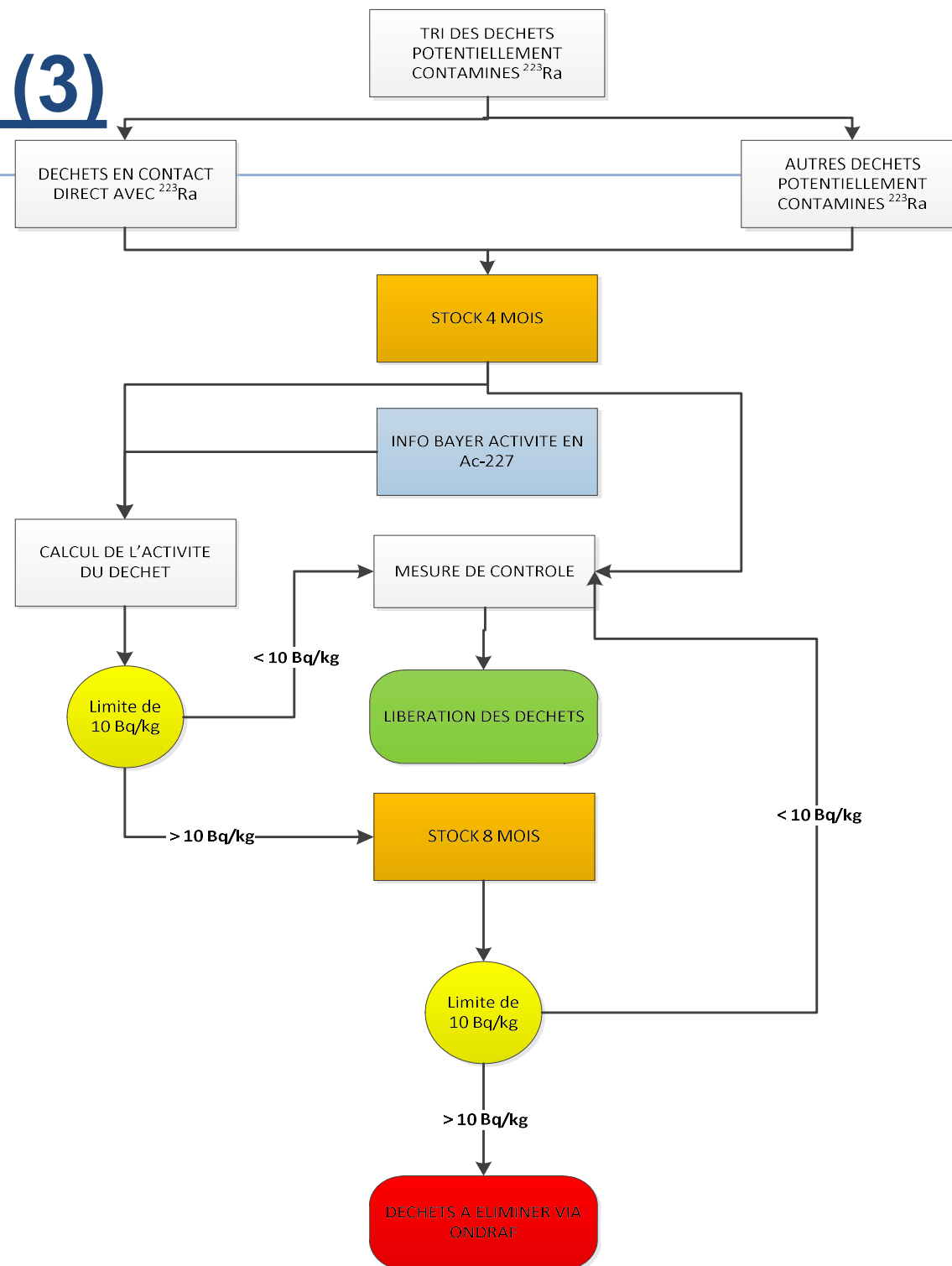
$$\text{Activity (Bq)} = X \times Y.$$

In the absence of a precise value from Bayer (LoD = limit of detection), the specific activity taken into account = 0.68 Bq/ml.

The activity of the waste can then be calculated on the basis of the weight of the waste (kg):

$$\text{Activity of the waste (Bq/kg)} = \text{Activity (Bq)} \times \text{Weight (kg)}$$

5. Wastes (3)



5. Wastes (4)

Gestion des déchets produits lors des traitements ²²³Ra.

Conformément au point 6.11. de la procédure Erasme-102-20 "Procédure d'utilisation du ²²³Ra dichlorure (Xofigo®) au Service de médecine Nucléaire", une revue et une mesure des déchets de traitements ²²³Ra a été effectuée ce jour.

Le 19/01/2017, nous avons reçu de la société Bayer, les informations concernant les concentrations en ²²⁷Ac dans les lots de ²²³Ra suivants (LOD : 0.023 Bq/ml) :

Clinical batch
C00192A
C00196A
ET10654B
ET10668B
ET10681A
ET10969B
ET10722B

Le préposé à la surveillance (B. Collette) a effectué les calculs prévus dans la procédure et résumés ci-dessous.

Identification du déchet	Activité massique max en ²²⁷ Ac (Bq/kg)	Proposition du préposé à la surveillance
C00192A – 06/03/2017	0.26	< 10 Bq/kg → A libérer
C00196A – 03/04/2017	0.36	< 10 Bq/kg → A libérer
ET10654B – 03/04/2017	0.17	< 10 Bq/kg → A libérer
ET10668B – 11/04/2017	0.11	< 10 Bq/kg → A libérer
ET10681A – 03/05/2017	0.13	< 10 Bq/kg → A libérer
ET10969B – 08/05/2017	0.13	< 10 Bq/kg → A libérer
ET10722B – 06/06/2017	0.13	< 10 Bq/kg → A libérer

Le SIPP-CP valide ces calculs et a procédé aux mesures suivantes :

Par ailleurs, les sacs de déchets reprenant le matériel qui n'a pas été en contact direct avec le Ra-223 (gants, alèzes, benchcoat,...) (6.11 2.b e la procédure) ont également été mesurés.

Identification du déchet	Mesure (1)	Décision du SIPP-CP
Pot à aiguilles + sac (06/03/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (03/04/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (03/04/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (11/04/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (03/05/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (08/05/2017)	≤ 120 c/s	Déchet peut être libéré
Pot à aiguilles + sac (06/06/2017)	≤ 120 c/s	Déchet peut être libéré

(1) Mesure bruit de fond compris ; le bruit de fond était de 120 c/s



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6. Incident (1)

22/02/2016 – 11:00 h: Patient managed by **Hospital A** receives a 1st Xofigo treatment (5.08 MBq) in Hospital B. The patient leaves **Hospital B**.

14/03/2016: The patient is hospitalised in **Hospital B** for complications.

22/03/2016: The patient receives his 2nd Xofigo treatment (5.22 MBq), then leaves Hospital A.

12/04/2016: The patient dies in **Hospital A**.

14/04/2016: Hospital B is notified of the death and planned cremation (!!). The RPE informs the FANC.

15/04/2016: The FANC publishes an Order that appoints Notified Body to manage the problem:

- Radioactivity that must be taken into consideration given the cremation and the collection of the ashes to be kept at home, etc.
- Cremation authorised in the presence of Notified Body
- Measurement and temporary storage of the ashes

Investigation conducted by the FANC: **Hospital A** was censured for not having fulfilled all its legal obligations with regard to compliance with the RGPRI.

Feedback proposed by Hospital B RPE: Establishment of a federal system for traceability of “injected” (or other) patients, with restrictions in the event of death.

7. Conclusions

- Xofigo is a treatment making use of ^{223}Ra (α emitter)
- Problems of contamination + and irradiation –
- Waste management +++
- Management of hospitalisation and death +++
- Necessity of excellent cooperation between MPE – RPO – RPE (and nursing – medical staff)

