The management of new radionuclides in clinical trials: radiopharmacy perspective

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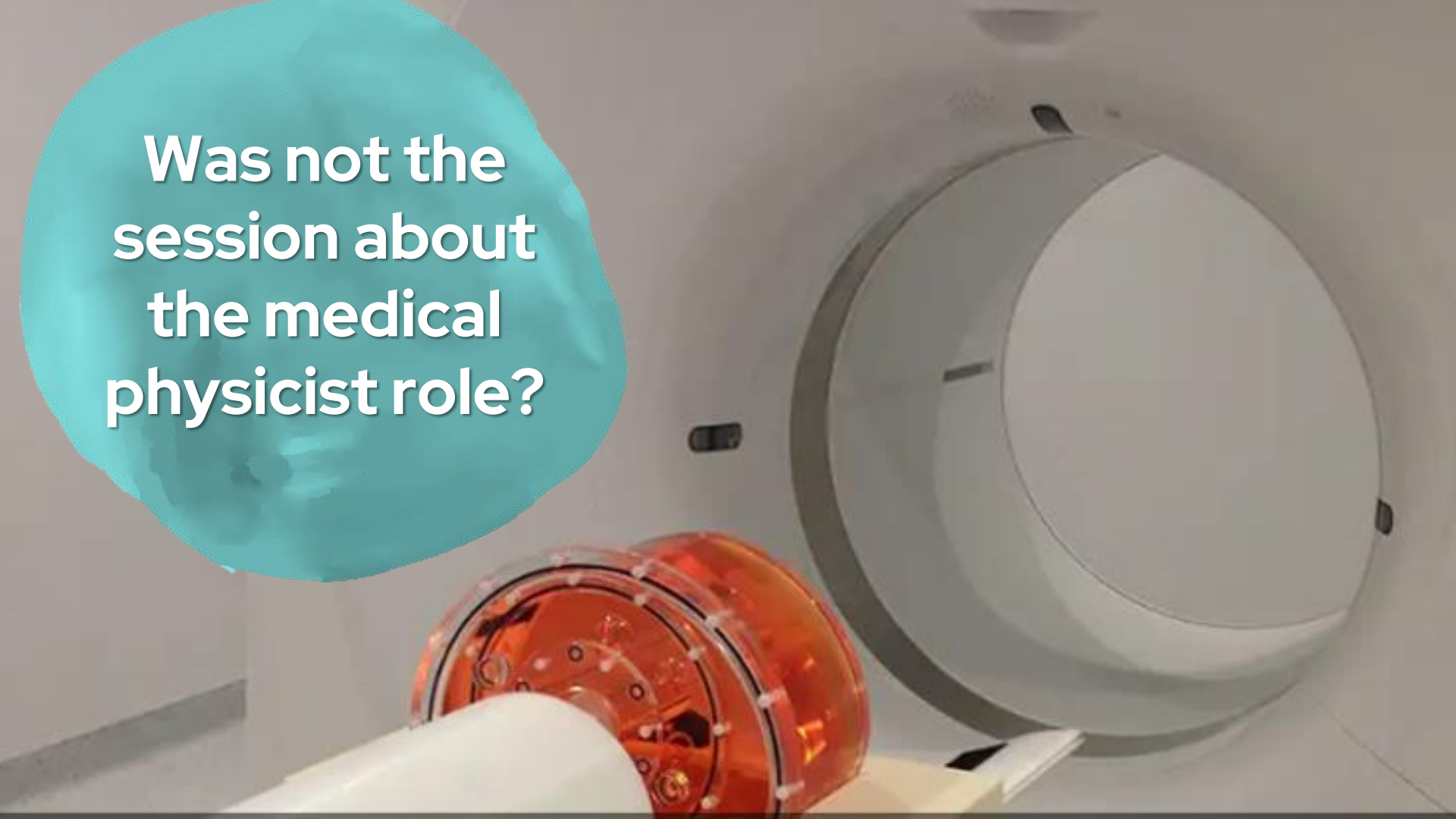
Was not the session about the medical physicist role?

Dr. Verónica Morán

Head of the Radiation Protection
Clínica Universidad de Navarra, Madrid, Spain

Since I am a Radiopharmacist...

...maybe we can talk about Radiation Protection of new radionuclides from the perspective of who need to apply all the protocols.

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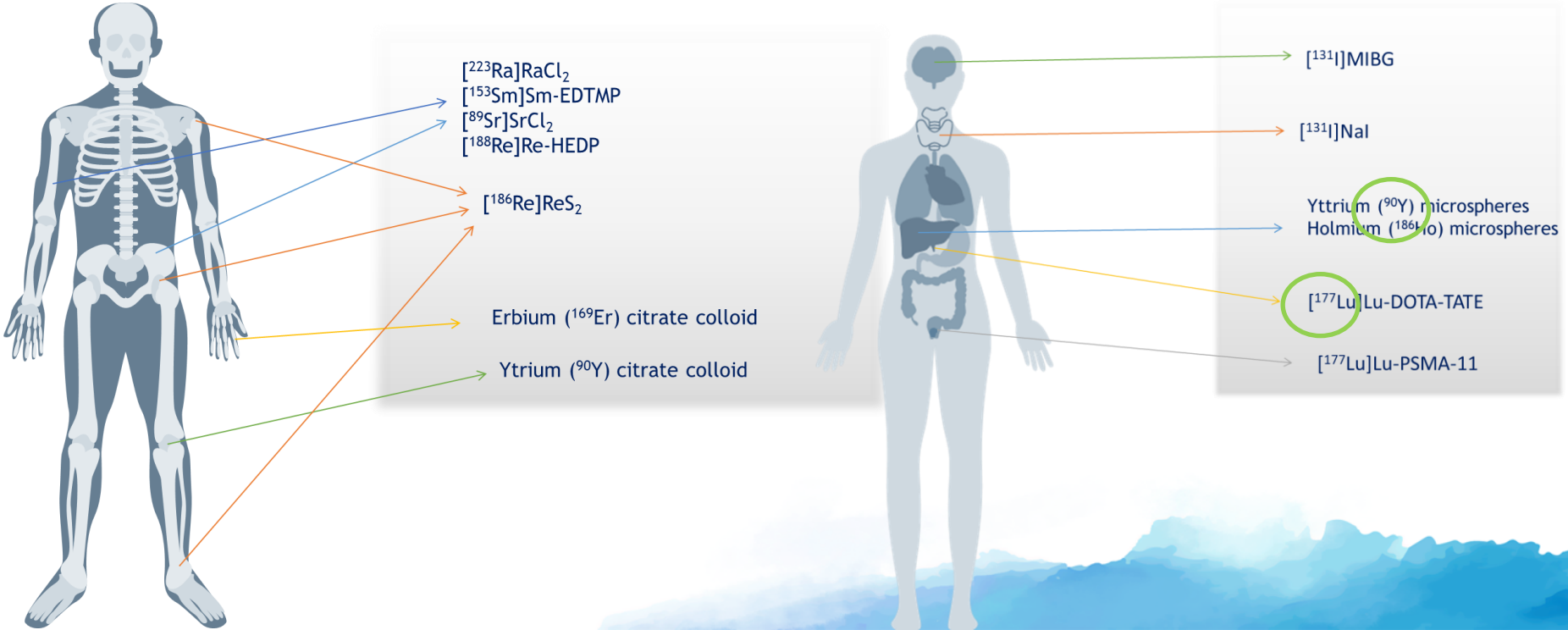
01 Radionuclides for Therapeutic Applications

Well stablished and new ones.

01 Radionuclides for Therapeutic Applications: well stablished.

The **use** of **radionuclides** in the **radiopharmacy field has existed** for **many years, but** the **last decades some** of them **are gaining attention** due to the **potential** for **prolonging patient survival** across **differing cancer types**, often with **minimal toxicity** for **healthy tissue**. **Almost all** of them are **β-emitters.**



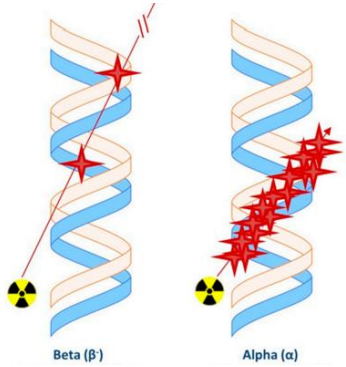
01 Radionuclides for Therapeutic Applications: new radionuclides

The **new radionuclides** are **alpha emitter**

α-emitter vs. β-emitter

- ❖ Superior cytotoxicity
- ❖ +++ Energy deposition per distance unit
- ❖ Limited range in tissue (0,1 mm)

Treatment of micrometastasic disease



^{177}Lu

β-particles

7,4 GBq

0,498 MeV/Bq.s

^{225}Ac

4 α-particles +2 β-particles

8 MBq

27.7 MeV/Bq.s

^{224}Ra

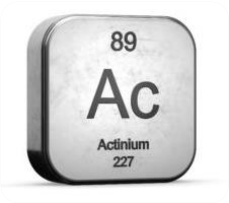
4 α-particles + 2 β-particles

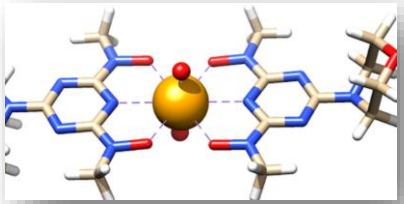
7 MBq

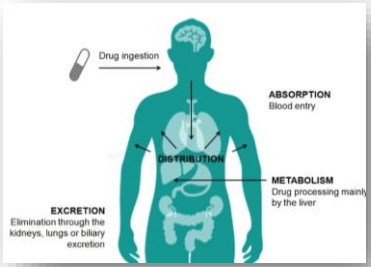
29,26 MeV/Bq.s

To deliver therapeutic absorbed doses at low administered activity levels

01 Radionuclides for Therapeutic Applications: actinium-225







Actinium is attached by a chelating moiety integral to the molecule (vector)

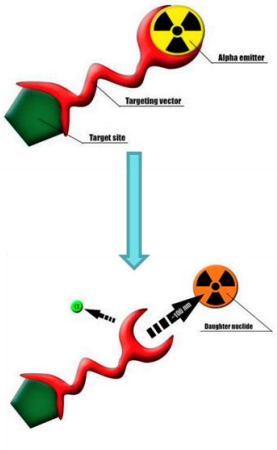
This chemistry is **similar** as the **Lutethium or the Yttrium** but **not exactly** the **same.** The use of **different radiometal** generally implies the need to use **different chelators.**

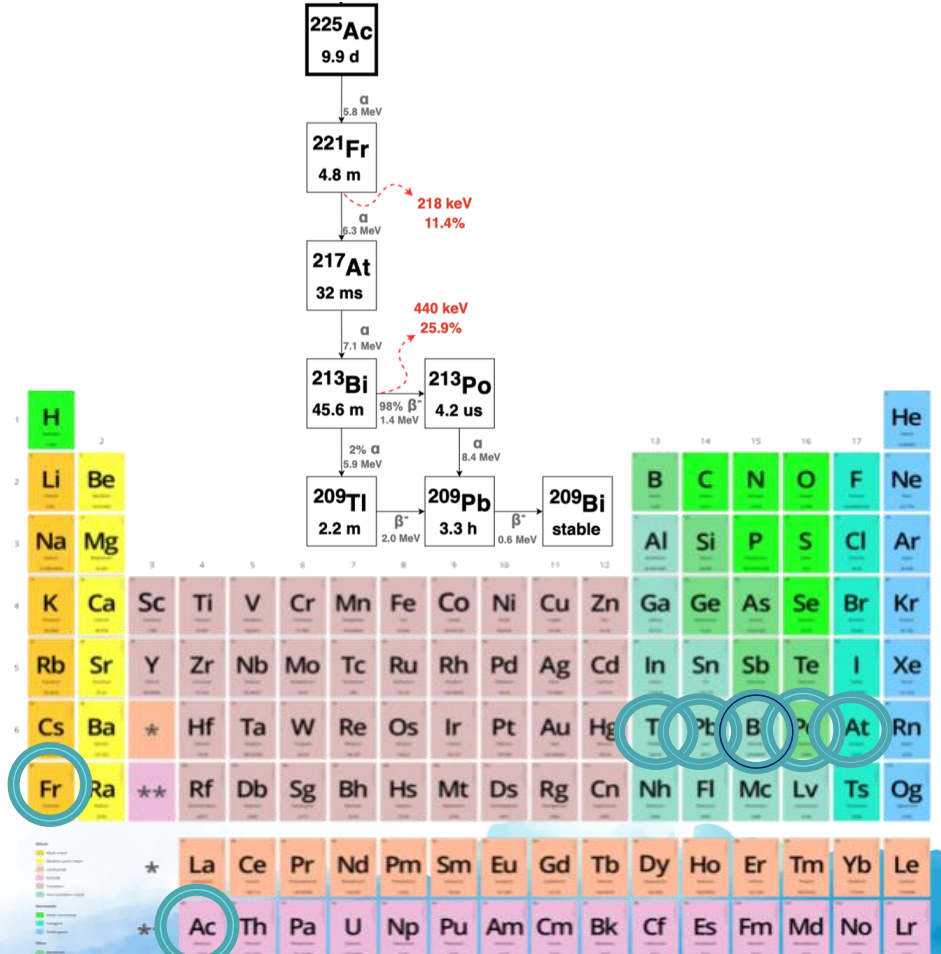
The use of **different chelators may implies changes** in the **the pharmacokinetic** of the **complex** in vivo.

The **isotopes produced during** the **decay** have to be also **chemically compatible** to the **chelator** of the actinium **to remain attached** to the molecule.

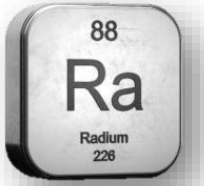
01 Radionuclides for Therapeutic Applications: actinium-225

The radioisotope produces during the decay are CHEMICALLY different from the actinium-225.
The BIOLOGICAL behavior is different.
The capacity of stay chelated of this isotopes is questions.
Possible adverse effects for irradiating healthy tissues.

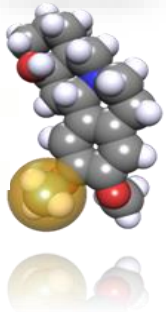




01 Radionuclides for Therapeutic Applications: Radium-224

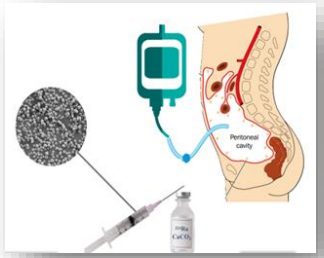


Radium isotopes has been **mainly used** to **bone-seeking applications**



Radium-223 has been the **most commonly used** for **clinical purposes** in the **last few years.**

Usually used in **inorganic solution because** of the **lack of** an **appropriate chelating agent** for coupling of radium to targeting molecules



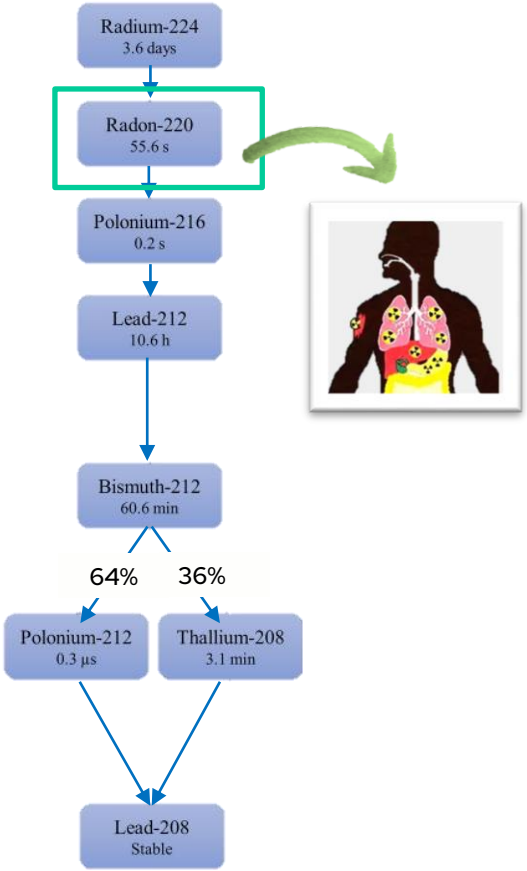
One proposed strategy is to use nanoparticles or micro particles as carriers.
$CaCO_3$ is an inorganic material that is promising for different biomedical applications.
Administration in ICU (after cytoreductive surgery)

[^{224}Ra]RaCaCO$_3$

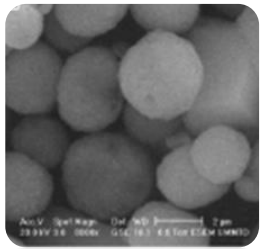
(Radspherin®)

2 Clinical Triails in Europe

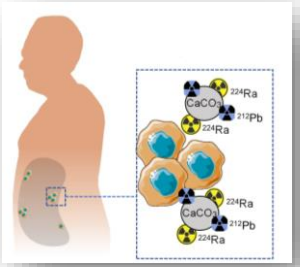
01 Radionuclides for Therapy Applications: Radium-224



- $CaCO_3$ insoluble → ^{224}Ra and progenies are trapped
- $CaCO_3$ dissolves in the peritoneum → ^{224}Ra is released
- $T_{1/2}(^{220}Rn) \sim s$ → Absorbed into the tissue



- Radioactivity in blood and urine ≈ Ø
- Fluid leaks from catheters or drains → Radioactive waste
- Low probability of ^{220}Rn release from peritoneum



02 Radiation Protection

Working with radium-224: our own experience

02 Radiation Protection: working with radium-224

The **$CaCO_3$ increase** the **solubility in H_2O, liberating the Radium-224 to the solution.**
During manipulation a contamination or even a vial break could occur, increasing the probability of Radon-220 liberation to the atmosphere

	Dose coefficient mSv/MBq
Ingestion	65
Inhalation	2900

Radiopharmacy and ICU staff (inhalation): % 224Ra released ??????????

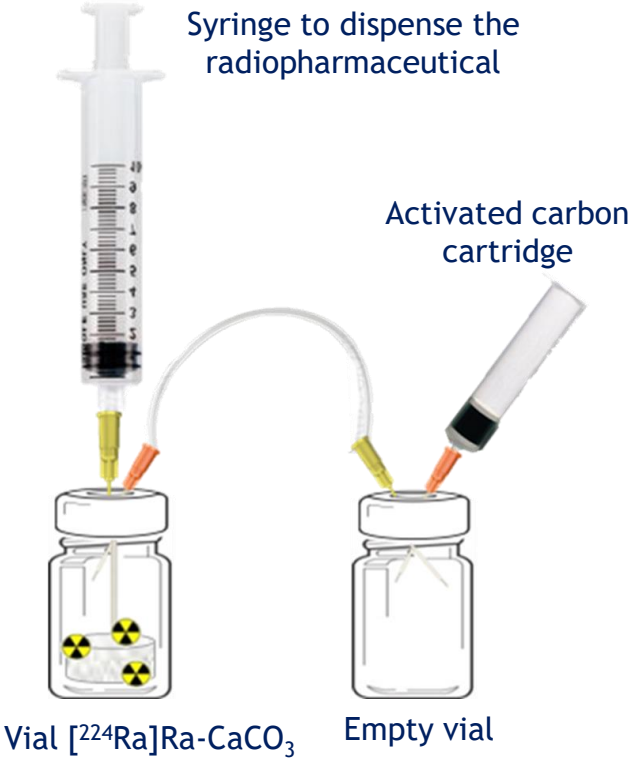
In order to prevent internal contamination: MANDATORY

Disposable clothing

Coal filter-gas mask

Laminar flow with minimal recirculation

02 Radiation Protection : working with radium-224



02 Radiation Protection: : working with radium-224

Distance (m)	Dose Rate in air (uSv/h)
0,1	20
1,0	0,2

Patient Dose Rate (@ 10 cm):

13,4 (10,9 – 16,8) uSv/h

Personal dose estimation

Irradiation risk

- **Radiopharmacy staff** (activity preparation):
  - Distance: 20 cm
  - Time: 1 h
  - N treatments: 1/week

  5 uSv/treatment → 0,25 mSv/year

20 mSv/y

- **Caregivers (ICU staff):**
  - Distance: 10 cm
  - Time: 24 h (since the treatment administration)
  - N treatments: 1/week

  13 uSv/treatment → 0,65 mSv/year

1 mSv/y

NO radiation dose limit is exceeded

Thank You!

Do you have any questions?

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