

Study on Sustainable and Resilient Supply of Medical Radioisotopes in the EU

Therapeutic radionuclides



Some key results and recommendations presented by Chiel Scholten



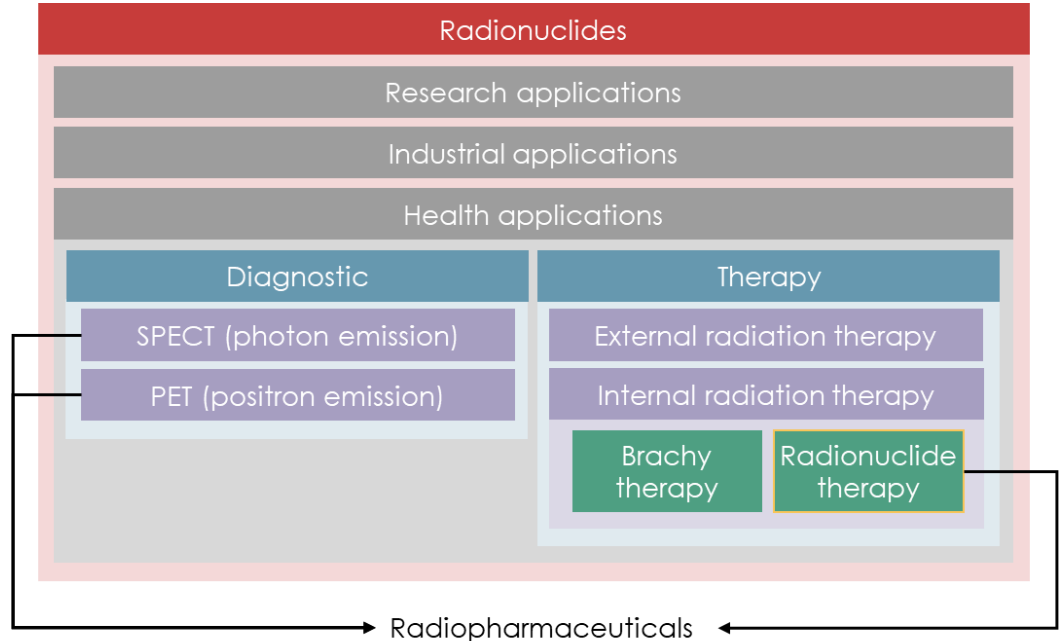
About the SMER2 study

- Commissioned by the **JRC** following calls for action from the Council of the EU
- **Mission:** provide insights in the use of RNs for medical therapy in the EU27 + UK
 - To also assess issues related to the sustainable and resilient supply of therapeutic radionuclides in the EU
- Publishable report: only rely on **public information**
- **Today:** key findings with a focus on use, trends and challenges



Scope of the SMER2 study on medical radionuclides

- The SMER2 study focused on **radiopharmaceuticals for radionuclide therapy**
- Here radionuclides are used for **targeted therapy** of various diseases, predominantly **cancer**
- Some radionuclides used in radionuclide therapy are imageable as well, these are called **tharagnostics**





Diagnostic vs. therapeutic radionuclides markets

- ↗ The market for therapeutic radionuclides is
 - ↗ much smaller (~100x)
 - ↗ much more volatile
 - ↗ growing faster
 - ↗ having higher margins

than the market for diagnostic radionuclides

- ↗ The last decade interest in radionuclide therapies has increased
 - ↗ new products entered the market (^{177}Lu -DOTATATE in 2017, ^{223}Ra -Cl₂ in 2013)
 - ↗ large pharmaceutical companies stepped in (Novartis, Bayer)
 - ↗ many R&D-activities on targeted radionuclide therapy worldwide
- ↗ The development of the market for therapeutic radionuclides is driven by therapeutic potential and the promise of growth in demand

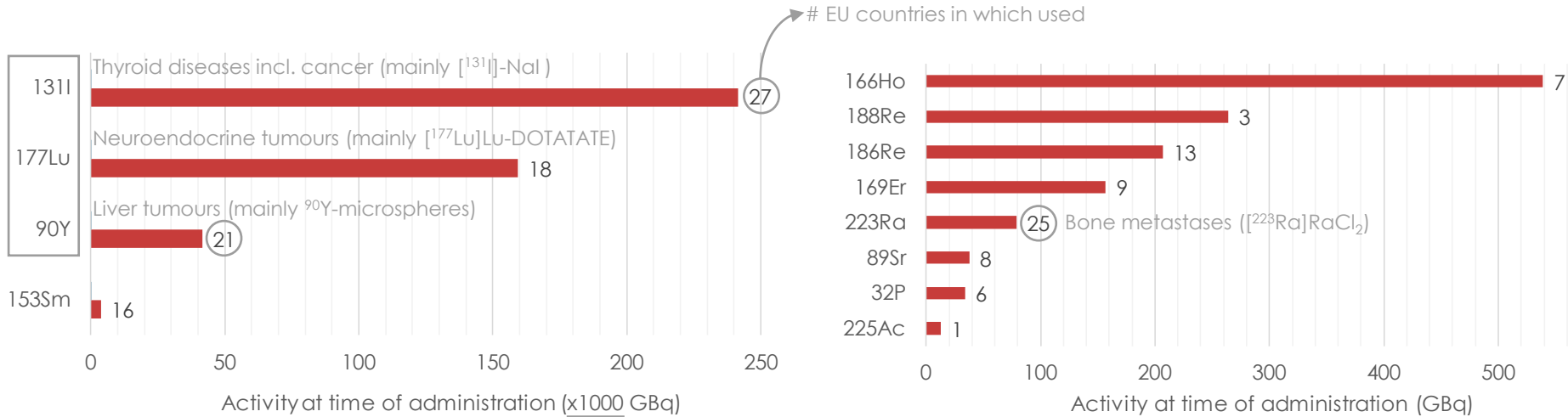
Radionuclides are used/tested for various indications

Radionuclide		Indications for use (in Europe)
³² P	β	Myeloproliferative disease and bone metastases
⁴⁷ Sc*	β	Under investigation for liver metastases
⁶⁷ Cu*	β	Under investigation for meningioma and neuroblastoma
⁸⁹ Sr	β	Bone pain palliation arising from skeletal metastasis
⁹⁰Y	β	Intra-arterial treatments in the liver, radiation synovectomy, B-cell and non-Hodgkin lymphoma, NETs
¹³¹I*	β	Benign thyroid diseases, thyroid remnant ablation, thyroid cancer, neuroblastoma and NETs
¹⁵³ Sm	β	Bone metastases
¹⁶⁶ Ho	β	Intra-arterial treatment in the liver, head/neck squamous cell carcinoma, hepatocellular carcinoma, bone metastasis
¹⁶⁹ Er	β	Radiation synovectomy
¹⁷⁷Lu*	β	Non-Hodgkin lymphoma, neuroendocrine tumours, castration resistant prostate cancer (pc), pc-metastases
¹⁸⁶ Re*	β	Radiation synovectomy
¹⁸⁸ Re	β	Non-melanoma skin cancer, painful bone metastases
²¹¹ At*	α	Under investigation for a range of tumours
²¹² Pb	β	Under investigation for a range of tumours
²¹³ Bi*	α, β	Under investigation for a range of tumours
²²³Ra	α, β	Castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastases
²²⁵ Ac	α, β	Metastatic castration resistant prostate cancer, acute myeloid leukemia
²²⁷ Th	α	Non-Hodgkin lymphoma, ovarian cancer, mesothelioma, metastatic castration resistant prostate cancer

(* = theragnostic)



Current European RN demand in terms of activity

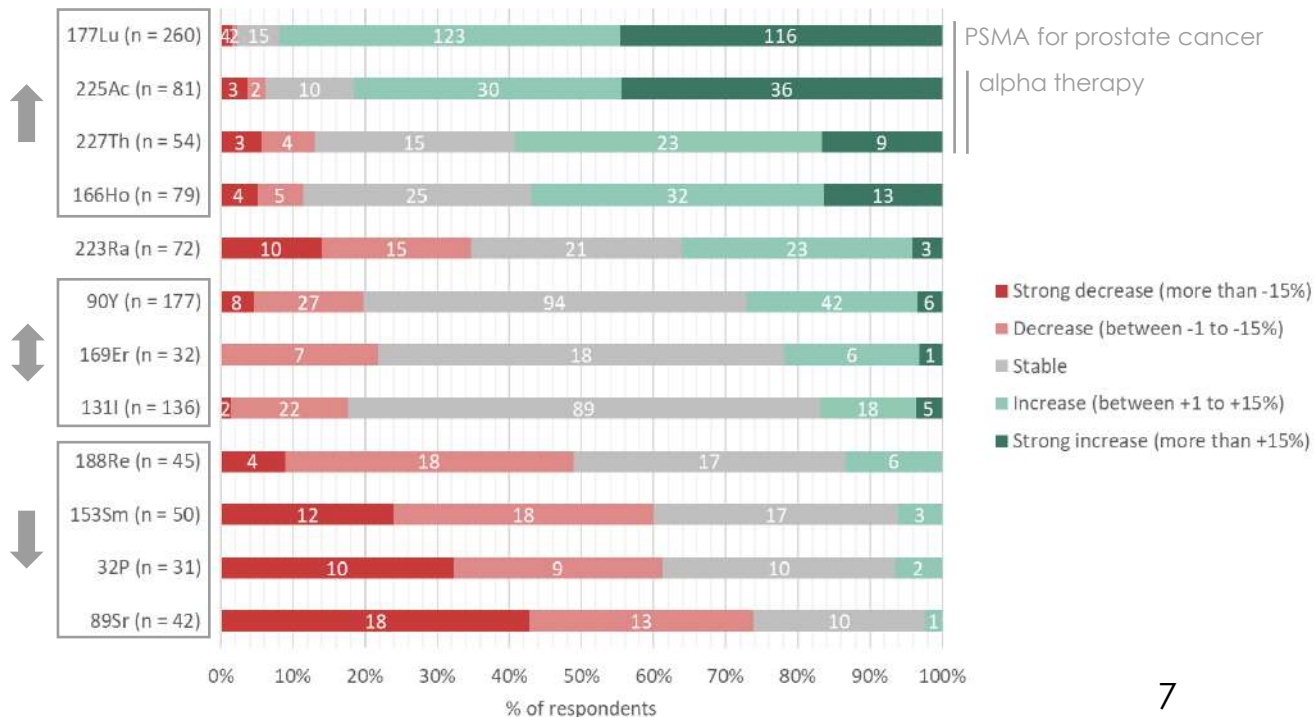


Expected radionuclide demand development in 10 years according to experts across the EU (survey)

Market for therapeutic RNs much more volatile than for diagnostic RNs

Demand for PSMA RPs expected to increase strongly

Increase also expected for several alpha emitters

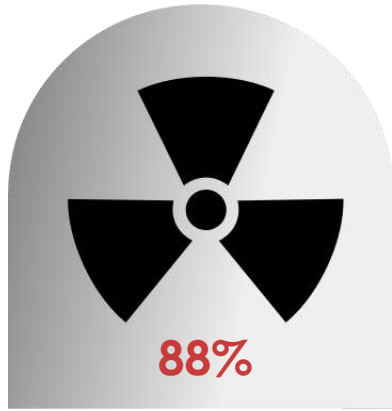


Incidence statistics show market potential

Therapeutic area(s)	Radiopharmaceutical	Average annual incidence rate in EU per 100,000 people	Absolute incidence in EU
Prostate	177Lu-PSMA; 225Ac-PSMA; 227Th-PSMA	171*	376,671
Non-Hodgkin lymphoma	90Y-ibritumomab-tiuxetan; 227Th-conjugate; 177Lu-antibodies	19	84,276
Liver and intra-hepatic bile ducts	90Y-resin microspheres; 90Y-glass microspheres; 166Ho-microspheres; 166Ho-chitosan	15	68,121
Leukaemia	225Ac-Lintuzumab	14	62,467
Thyroid gland	131I-Nal	12	52,655
Endocrine and Brain and other CNS	131I-mIBG	10	41,977
Myeloma and Bones and Joints	32P-sodium-phosphate	9	37,565
Mesothelioma	227Th-antibody	2	10,096
Bones and joints	90Y-colloids; 89SrCl2; 223RaCl2; 188Re-HEDP; 186Re-colloids; 169Er-colloids; 166Ho-DOTMP; 153Sm-EDTMP	1	4,507
Endocrine	177Lu-DOTATATE	1	2,588

Data from ECIS, 2010, * = only male population

Most therapeutic RNs are most effectively produced using nuclear reactors, only a few with accelerators



Nuclear reactor: ^{32}P , $^{47}\text{Sc}^*$, ^{89}Sr , ^{90}Y ,
 $^{131}\text{I}^*$, $^{153}\text{Sm}^*$, ^{166}Ho , ^{169}Er , $^{177}\text{Lu}^*$,
 $^{186}\text{Re}^*$, ^{188}Re , ^{223}Ra , ^{227}Th

Generator/decay: ^{212}Pb ,
 $^{213}\text{Bi}^*$, ^{225}Ac

12%

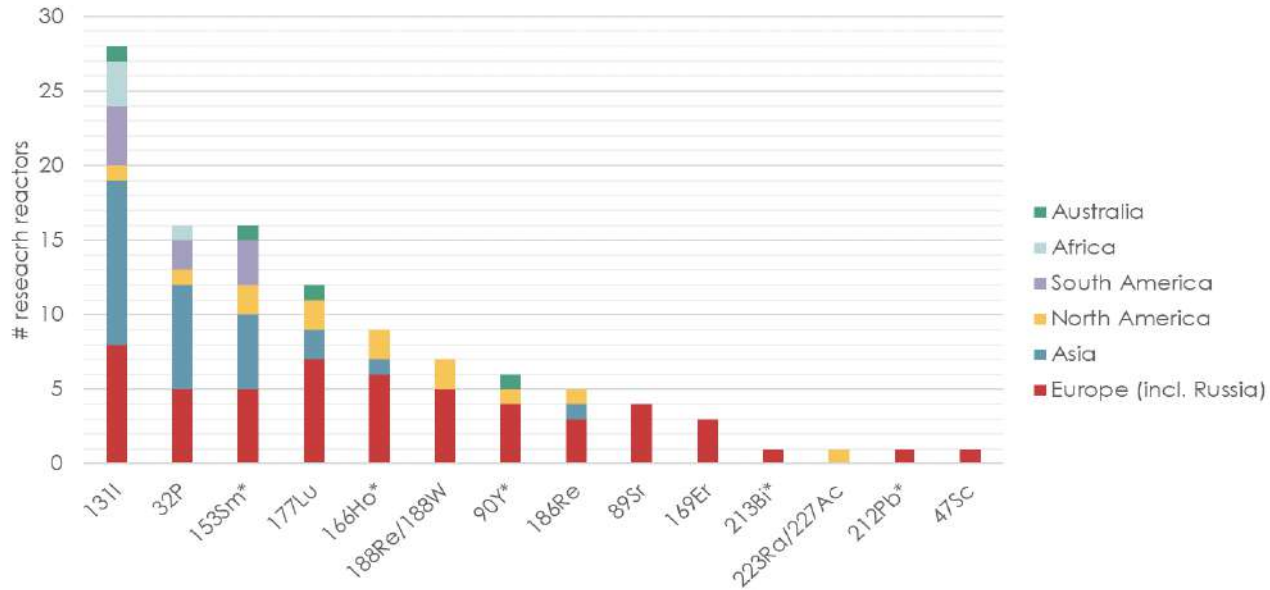


Accelerator/cyclotron:
 $^{67}\text{Cu}^*$, $^{211}\text{At}^*$, (^{186}Re),
(^{223}Ra), (^{225}Ac)

(* = theragnostic)



RNs supplied by research reactors across the world

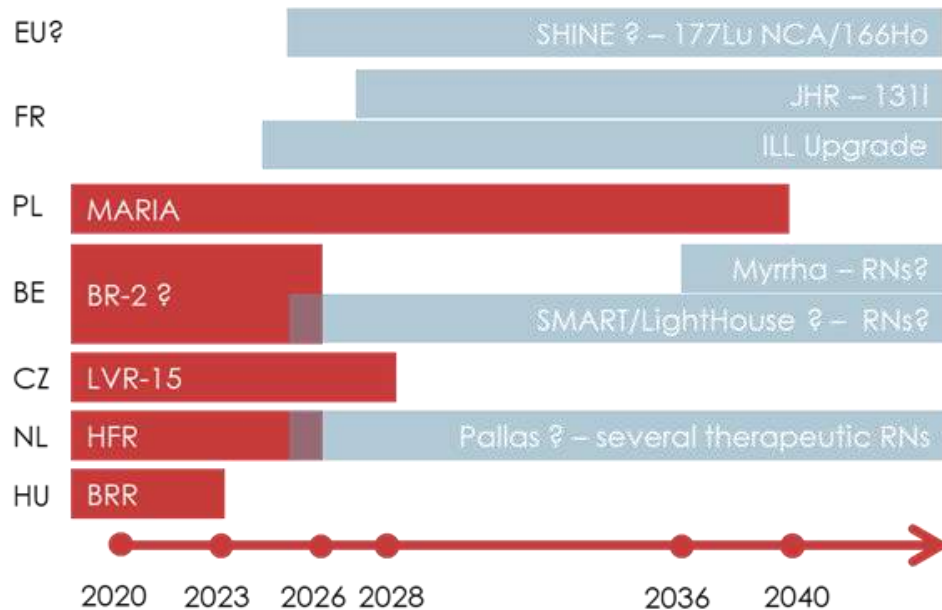


Based on most recent available data collected, no production volumes (!)

- ↗ Europe has currently multiple local suppliers for most therapeutic RNs often used to date
 - ↗ ²²³Ra seems exception
- ↗ 7 research reactors in EU produce most therapeutic RNs, most 50+ years old
- ↗ For most long-lived therapeutic RNs foreign suppliers exist
- ↗ Cyclotron-produced RNs studied have limited supply/few suppliers



In less than 20 years 5 European research reactors will stop operations, with some plans for new build

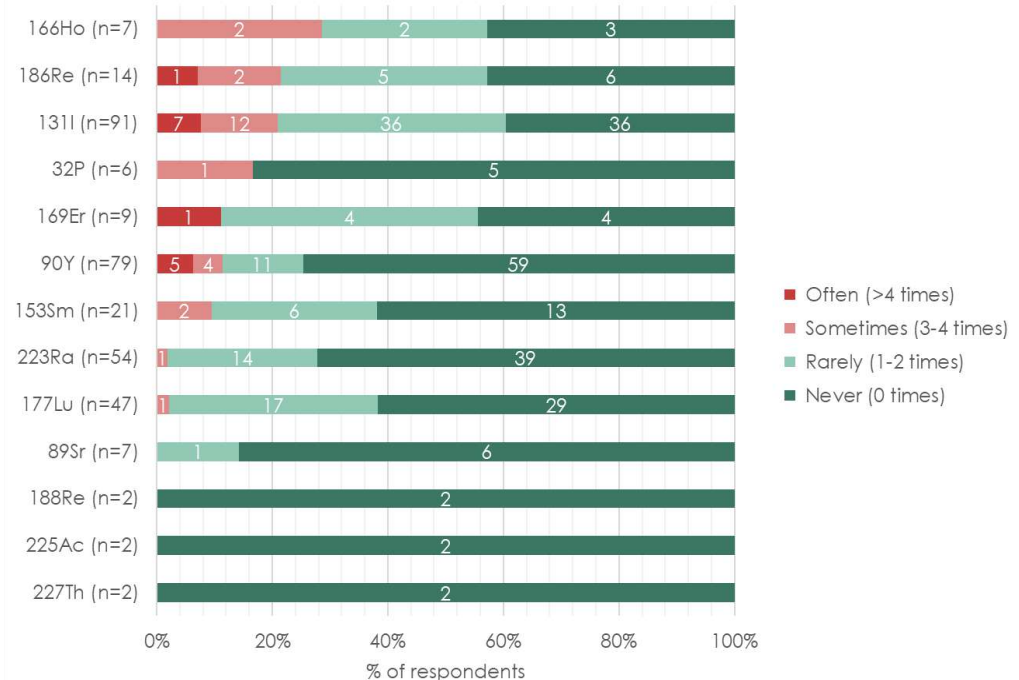


- ↗ Most planned new build in Europe uncertain in terms of:
 - ↗ Realisation – e.g. Pallas & Shine
 - ↗ Start of operations – dates shift
 - ↗ Therapeutic RNs produced – some have no clear plans or produce only some specific RNs
 - ↗ Innovation – novel concepts
 - ↗ Volumes – can replace current production capacity?
- ↗ Limited potential to increase current production capacity



Supply of therapeutic RNs fairly stable in past 5 years

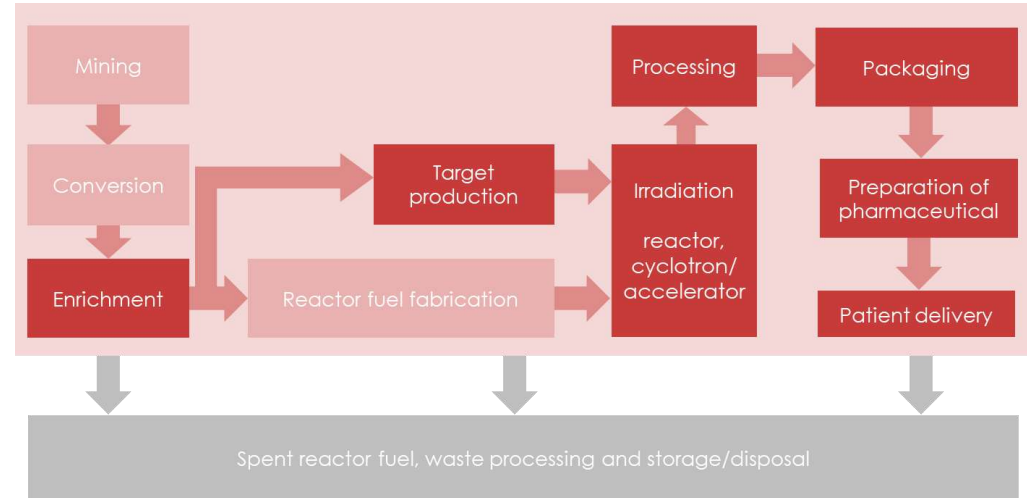
- ↗ Shortages of therapeutic RNs always impact the treatment of patients
- ↗ Commonly used RNs ¹³¹I and ⁹⁰Y are most reported as being often short in supply
- ↗ Causes vary, but most often during external production
- ↗ Transport weak spot during Covid pandemic





Current European RP supply chain seems adequate, but fragile, and not resilient

- ↗ Foreign dependencies in supply chain:
 - ↗ Raw material
 - ↗ Enrichment of LEU and stable isotopes (targets, esp. ^{176}Yb)
 - ↗ Ageing European reactors
- ↗ Meeting projected demand with supply for esp. ^{177}Lu seems impossible with current ageing installations





Key recommendations on demand and supply

- Concerted and urgent **action at EU level** is needed to **secure sufficient irradiation capacity** for therapeutics RNs in Europe in the future
- Decide politically whether Europe wants to be **self-sufficient in enrichment** to produce target materials and research reactor fuel
- Consider supporting public-private **R&I to strengthen future supply chain** for therapeutic RNs
- **Widen information-sharing** regarding supply capacities, new builds, demand expectations and outages for key therapeutic RNs
- Improve standardised **national data collection** on the use of RPs
- Stimulate R&I and training in RPs to **foster translation to clinic**



Get in touch!

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