CERN-MEDICIS :

research medical radionuclides

and

European programmes

Thierry STORA – CERN

Visit of delegation TEN/833 of EESC committee*

https://indico.cern.ch/event/1145660/

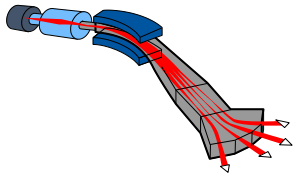
* The European Parliament, the Council and the Commission shall be assisted by an **Economic and Social Committee** (…) acting in an advisory capacity."

1957, Treaty on EU, Art. 13

Did you say ?

research radionuclides (production/purification)

in personalised medicine



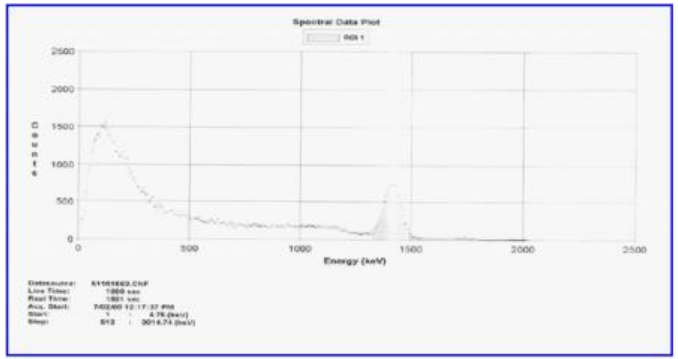
Radioisotopes in biological organisms

Daily, we “internalize” radiomarkers with rather well defined protocols

evian
Natural Spring Water

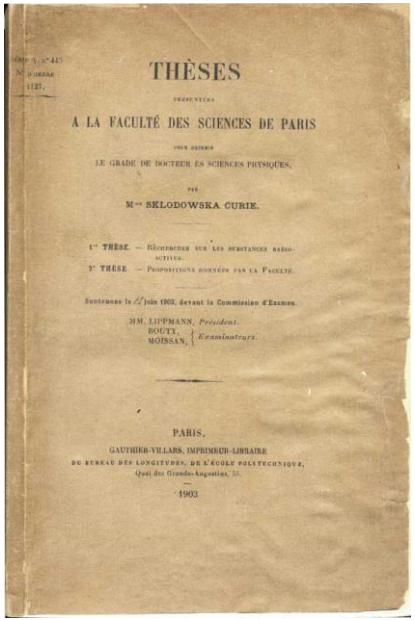
Country	France
Source	Évian-les-Bains
Type	still
pH	7.2
Calcium (Ca)	80
Chloride (Cl^-)	6.8
Bicarbonate (HCO_3)	360
Magnesium (Mg)	26
Nitrate (NO_3)	3.7
Potassium (K)	1
Silica (SiO_2)	15
Sodium (Na)	6.5
Sulfates (SO)	12.6
Website	http://www.evian.com

All values in milligrams per liter (mg/l)



M Goma et al

The early days



THÈSES

PRÉSENTÉES

À LA FACULTÉ DES SCIENCES DE PARIS

POUR OBTENIR

LE GRADE DE DOCTEUR ÈS SCIENCES PHYSIQUES,

PAR

Mme SKLODOWSKA CURIE.

1re THÈSE. — Recherches sur les substances radio-actives.

2e THÈSE. — Propositions données par la Faculté.

Soutenues le 25 juin 1903, devant la Commission d'Examen.

MM. LIPPMANN, *Président.*
BOUTY,
MOISSAN, } *Examinateurs.*

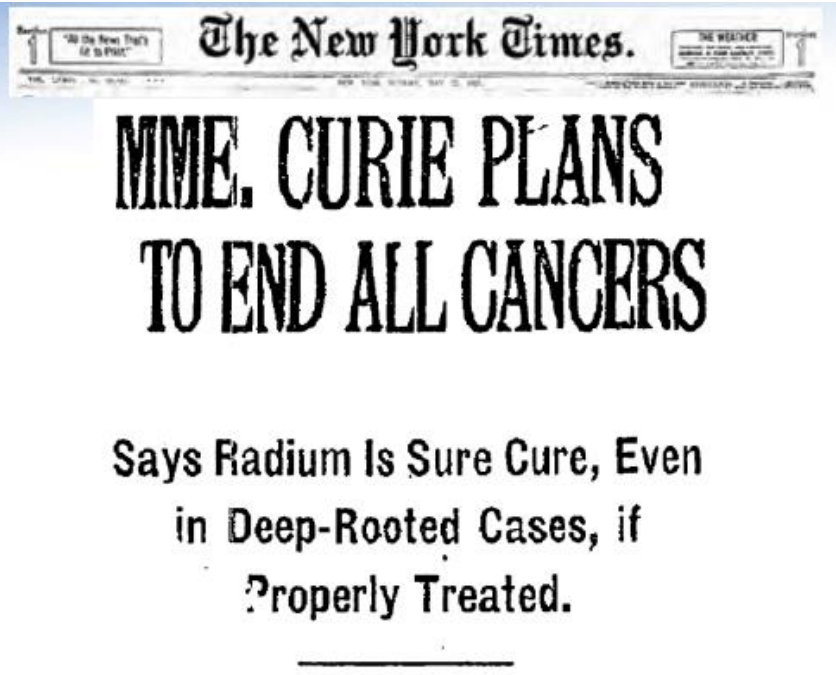
PARIS.

GAUTHIER-VILLARS, IMPRIMEUR-LIBRAIRE
DU BUREAU DES LONGITUDES, DE L'ÉCOLE POLYTECHNIQUE,
Quai des Grands-Augustins, 55.

1903

Marie Sklodowska-Curie
1867-1934

Published:
May 12th 1921
© The New York Times



The New York Times.

MME. CURIE PLANS TO END ALL CANCERS

Says Radium Is Sure Cure, Even in Deep-Rooted Cases, if Properly Treated.

Courtesy prof O. Ratib

While flying to a workshop in Manchester (in 2014)

While flying
to a workshop in Manchester

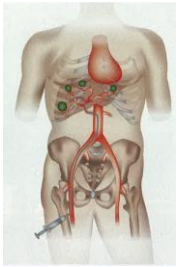

100 Advertorial

Mikrokugeln gegen Leberkrebs

Tiny beads used to treat liver cancer

Die Hirslanden Klinik St. Anna in Luzern führt eine neuartige Behandlung für Lebertumore durch, bei der hohe Strahlungsdosen mittels kleinster Kügelchen direkt in die Tumore injiziert werden.

Hirslanden Klinik St. Anna in Lucerne, Switzerland, provides a new high-dose radiotherapy treatment for liver tumours which works by injecting tiny beads straight into the tumours.



Leaver treatment with microspheres loaded with ^{90}Y

2015

AAA bought by Novartis for
3.8 Bi$ in 2017 (^{177}Lu-based drug)

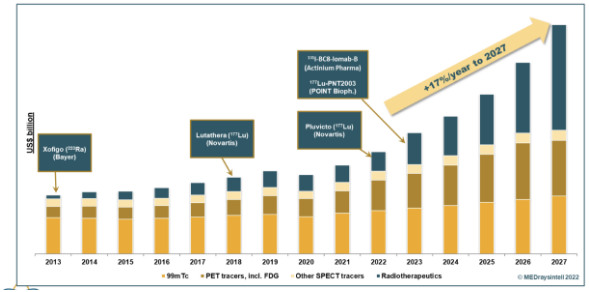
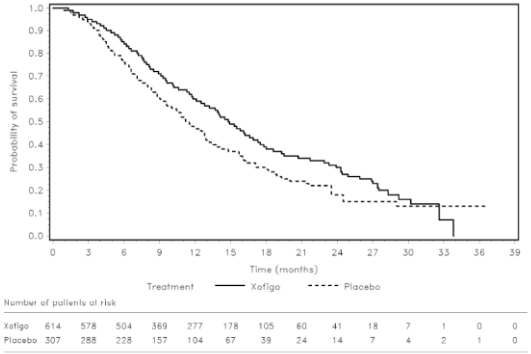
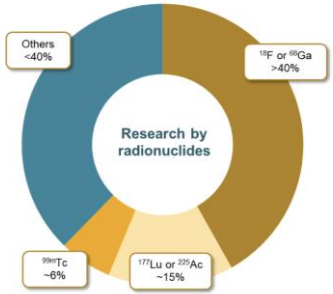


Figure 1 – Courbes de survie globale de Kaplan-Meier (analyse actualisée)





ALSYMPCA Phase III clinical trial
https://www.vidal.fr/medicaments/xofigo-1100-kbq-ml-sol-inj-164403.html

Courtesy Prof. Ratib

Example of theranostics concept in pre-clinical research

- PET 152-Terbium radionuclide in antibody-based targeted moleculer therapy

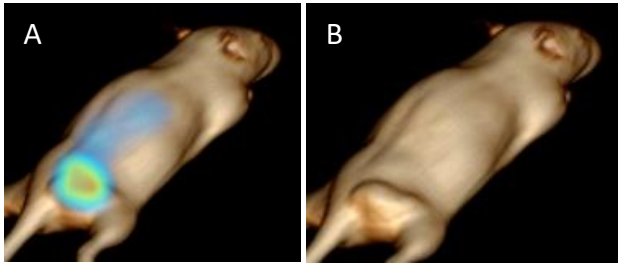
Diagnostics

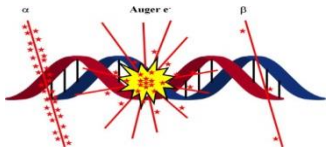
THERAPY

Cicone *et al. EJNMMI Research* (2019) 9:53
https://doi.org/10.1186/s13550-019-0524-7

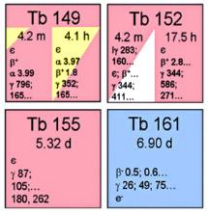
ORIGINAL RESEARCH Open Access

Internal radiation dosimetry of a ^{152}Tb-labeled antibody in tumor-bearing mice



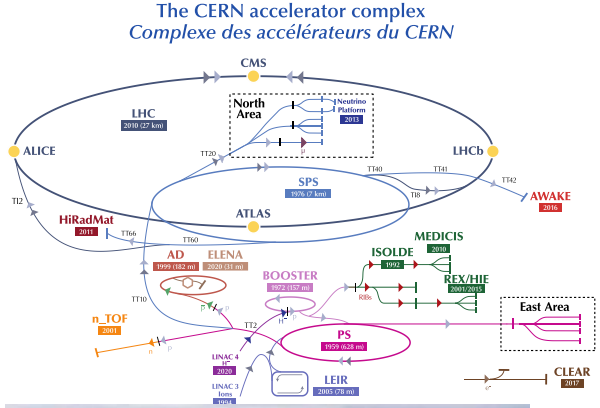


Matched therapeutic Tb

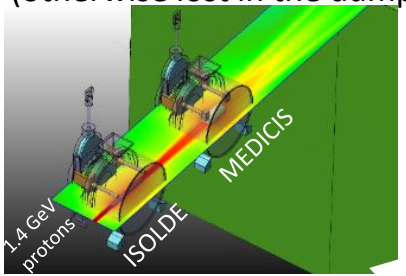


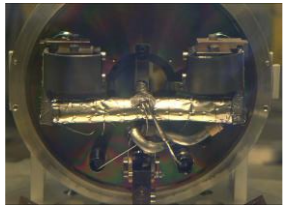
C. Müller et al., *Journal of nuclear medicine* 53.12 (2012): 1951.

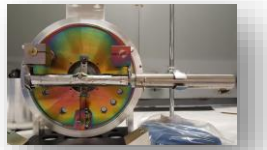
Mass separation as applied in MEDICIS in a snapshot



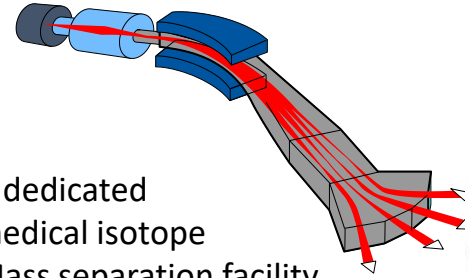
“Free” proton beam
(otherwise lost in the dump)



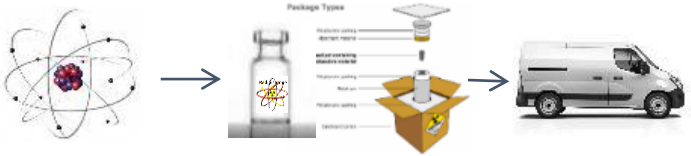




Cyclotron or reactor target transfer into Isotope mass separation unit



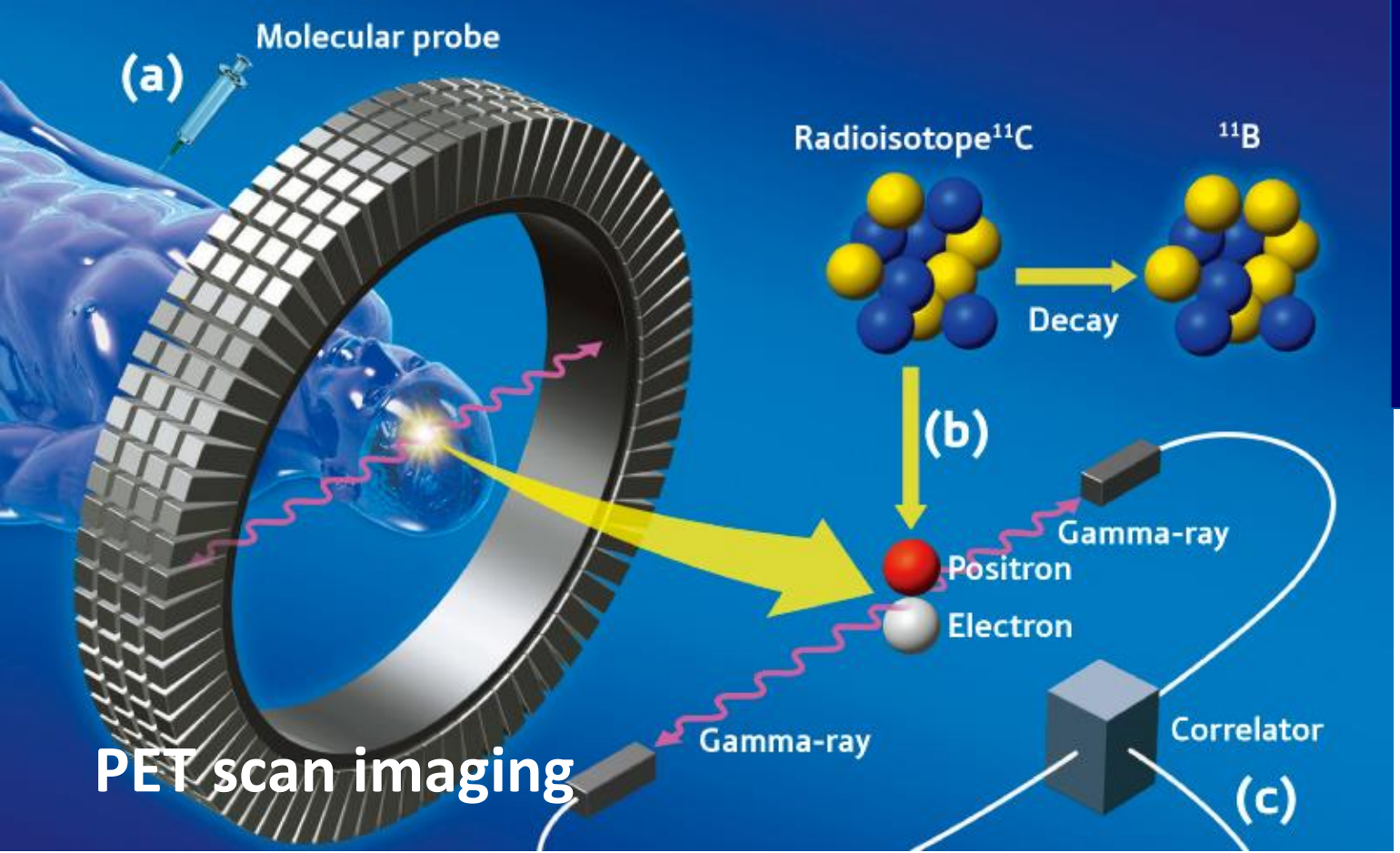
A dedicated medical isotope Mass separation facility in Europe.

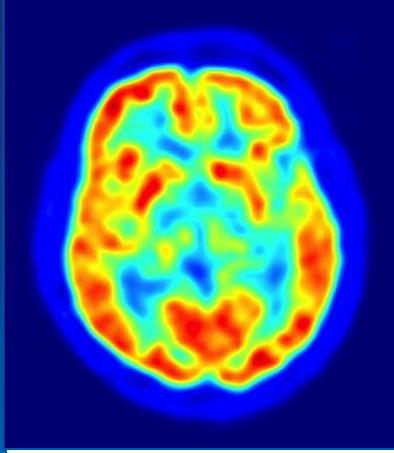


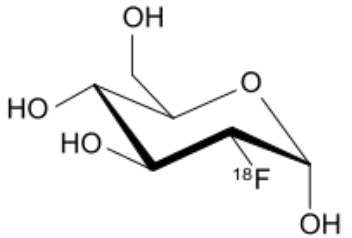
From CERN- MEDICIS to the lab/Hospital

Some **MEDICIS isotopes** :
High activity Sm-153, Ba/Cs-128, Tm/Er-165

PET scan imaging

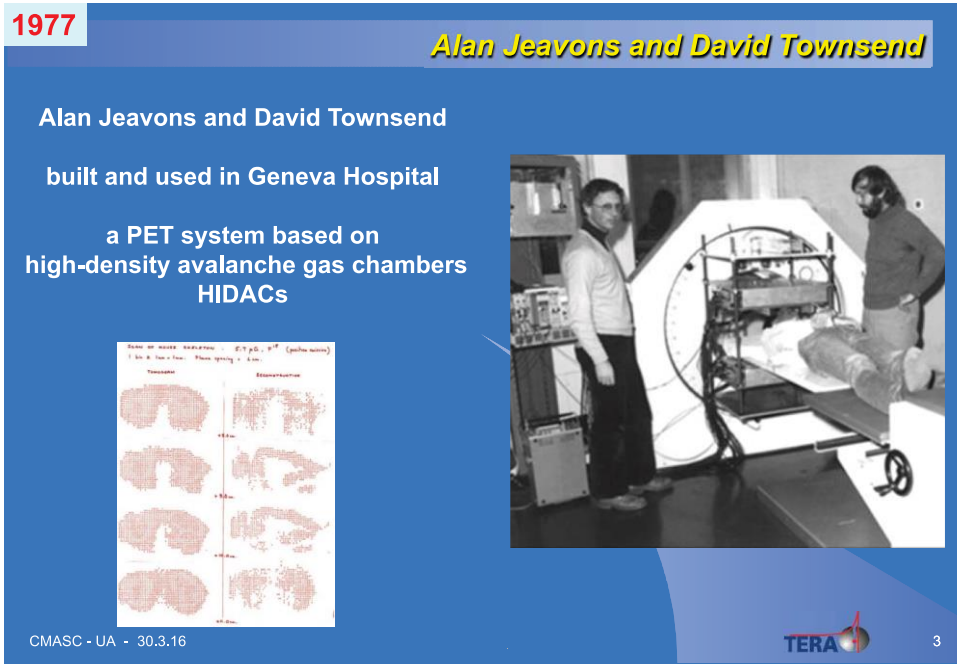


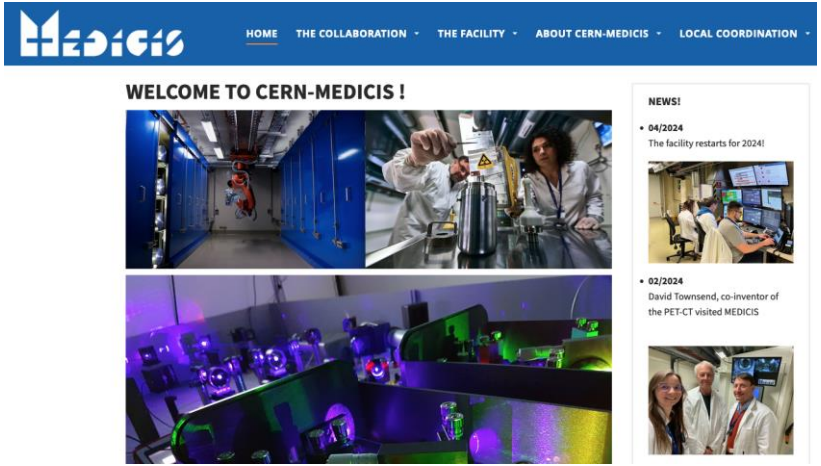




Fluorodésoxyglucose (^{18}F)

PET-CT scan imaging





Courtesy Ugo Amaldi

https://home.cern/news/news/knowledge-sharing/forty-years-first-pet-image-cern

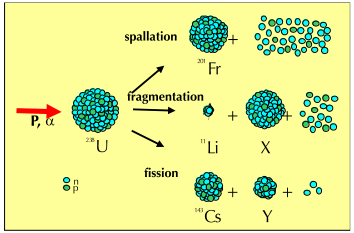
How to supply “novel” radionuclides with mass separation

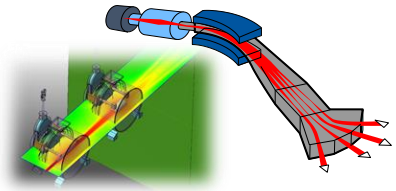
- **PRISMAP** proposes to federate a consortium of high energy cyclotrons, research reactors, and isotope mass separation facilities in Europe.

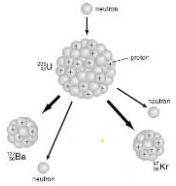
Accelerator

Isotope mass separation

Research reactor







$I_{[pps]} \sim F_{[pps]}\ S_{[barn]}\ N_{[g/cm2]}$ **production rate**

10^{10}pps 100∝A (6.10^{14}) 1mbarn 1g/cm² for A_{target}=30g/mol

$I_{[pps]} \sim F_{[pps]}\ S_{[barn]}\ N_{[g/cm2]}\ e_{[\%]}$

$$\frac{dN'}{dt} = nv\sigma_{act} N_T$$

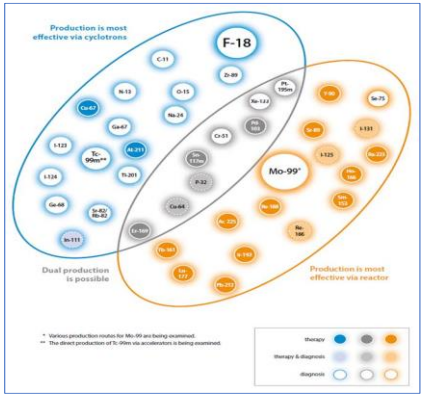
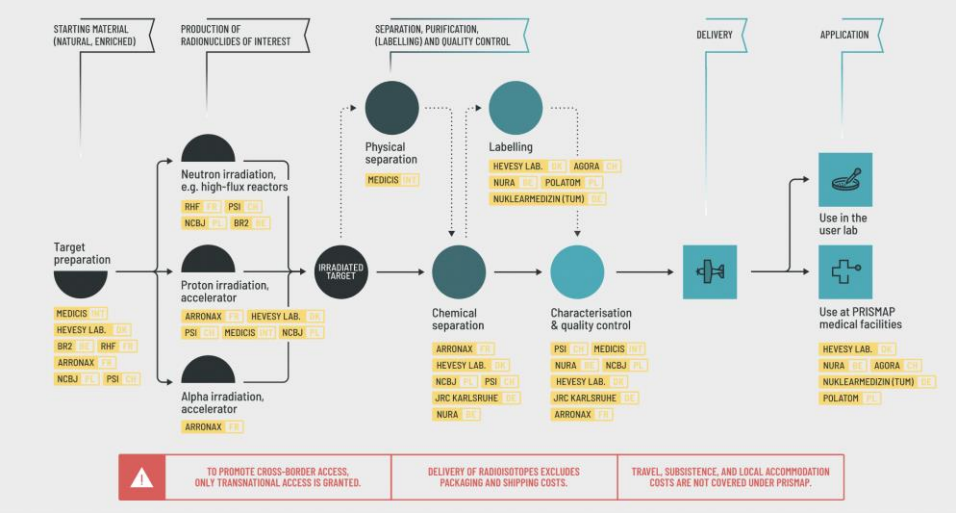
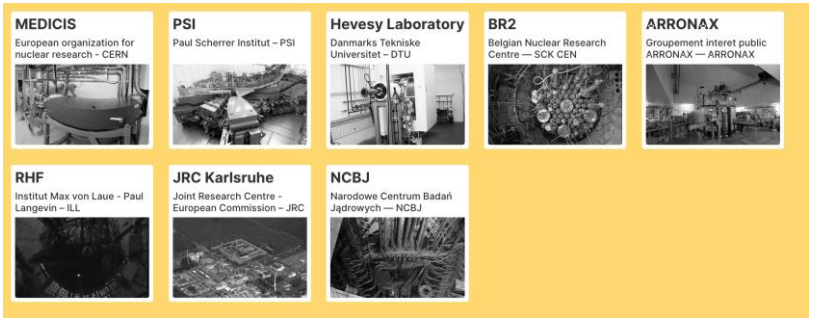


Figure 31 : Main medical radioisotopes production process

European Commission
ENER/17/NUCL/SI2.75566
0
(2018)

What is in the back of PRISMAP





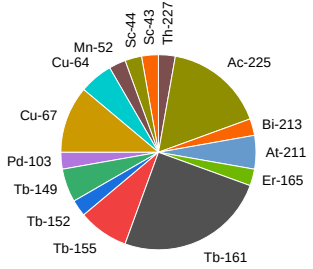
Our initial proposal for day-1 radionuclides

Table 1. PRISMAP day-1 radionuclides.

Radionuclide	Application	Imaging(I)/ Treatment(T)/ Generator(G)	Production reaction
Sc-44/Sc-44m	PET	I	^{44}Ca(p,n); ^{44}Ca(d,2n)
Sc-47	β⁻ therapy, SPECT	I/T	^{46}Ca(n,γ)^{47}Ca(β⁻)
Cu-64	PET	I	^{64}Ni(p,n); ^{64}Ni(d,2n)
Cu-67	β⁻ therapy, SPECT	I/T	^{68}Zn(p,2p); ^{70}Zn(p,α)
Ag-111	β⁻ therapy, SPECT, TDPAC	I/T	^{110}Pd(n,γ)^{111}Pd((β⁻); ^{110}Pd(d,n)
La-135	Auger therapy	T	^{nat}Ba(p,X)
Tb-149	α therapy, PET	I/T	^{nat}Ta(p,spall)
Tb-152	PET	I	^{nat}Ta(p,spall)
Tb-155	Auger therapy, SPECT	I	^{nat}Ta(p,spall)
Tb-161	β⁻ therapy, SPECT	I/T	^{160}Gd(n, γ)
Dy-166	Generator for Ho-166 (β⁻ therapy, SPECT)	G	^{164}Dy(n, γ)(n, γ)
Er-165	Auger emitter	T	^{165}Ho (p, n)
Tm-165	Generator for Er-165 (Auger therapy)	G	^{nat}Ta(p
Er-169	β⁻ therapy	T	^{168}Er(n, γ)
Yb-175	β⁻ therapy, (SPECT)	T	^{174}Yb(n, γ)
Pt-195m	Auger therapy, SPECT	I/T	^{194}Pt(n, γ)
Bi-213	α therapy	T	^{225}Ac generator
At-211	α therapy	T	^{209}Bi(α,2n)
Ac-225	α therapy	T	^{229}Th generator; ^{232}Th(p,spall)

And at call 4 :

→ www.prismap.eu/radionuclides/portfolio/224Ra/
→ www.prismap.eu/radionuclides/portfolio/203Pb/



PRISMAP in a nutshell

- Provide access to new radionuclides and new purity grades for the medical research
- Create a common entry port and web interface to the starting research community
- Enhance clarity and regulatory procedures to foster research with radiopharmaceuticals
- Improve the delivered radionuclide data and regulatio along with biomedical research capacity
- Ensure long-term sustainability of PRISMAP

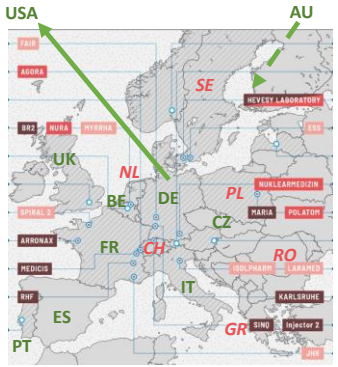
→16 non-conventional radionuclides (amongst the 28)

→ 31 research groups from 12 countries

→ 32 projects covering the different aspects of translational medical research.

User projects and services

In vivo cellular & molecular imaging lab (ICMI) VU Brussels Imaging and Pathology KU Leuven Molecular Imaging Center Antwerp	BELGIUM
Pharmaceutical Radiochemistry TU Munich Radiopharmaceutical Cancer Research Dresden (/CZ)	CZECH Rep. GERMANY
UGA – Inserm La Tronche Radiopharmacy Bordeaux CEMHTI Radiochemistry Orleans Radiochemistry Hopital Frederic Joliot Orsay Inserm Montpellier (/PT)	FRANCE PORTUGAL
Fondazione IRCCS Istituto Nazionale dei Tumori Milano Dep Molecular Biotechnology Health Sciences, Torino	ITALY
Radiochemistry unit, Hospital Gregorio Marañón Madrid	SPAIN
Biomedical Engineering and Imaging Science London	UK



https://www.prismap.eu/access/user-projects/

After call 4 :

x2 projects (16→ 33) 1→US

+50% countries (8→12 UK/CH)

Southern & Eastern (*) EC country

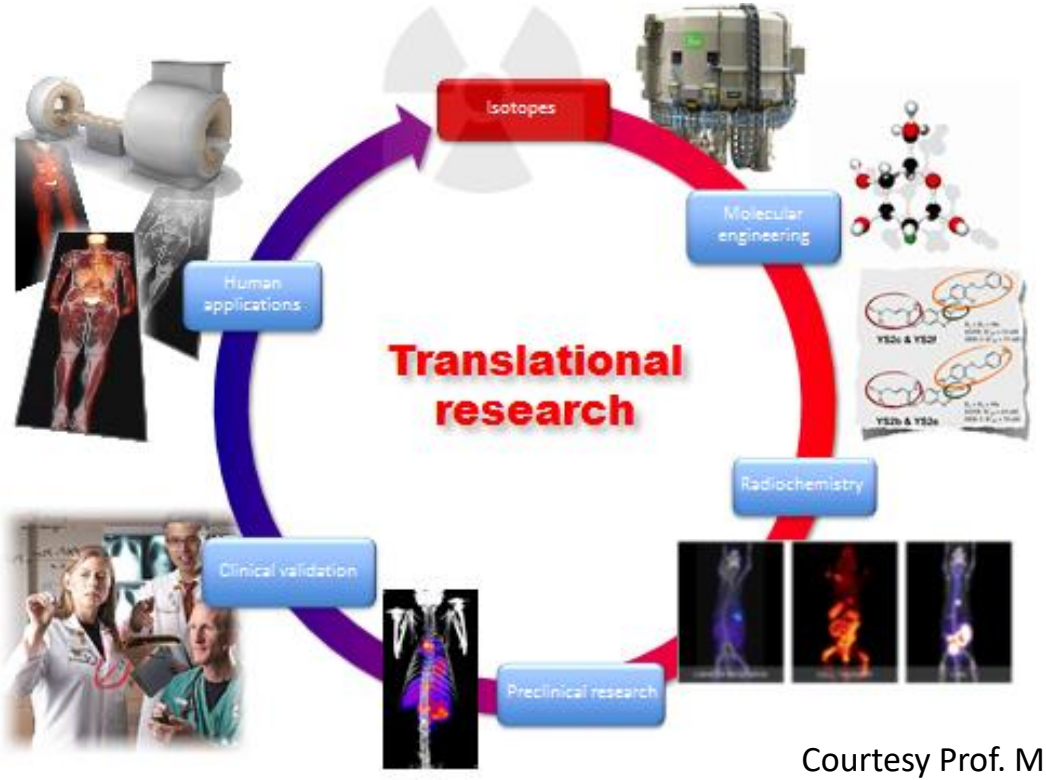
(W→ W,S,E+ Sweden most N)

35(*) research teams

Did you say ?

in personalised medicine

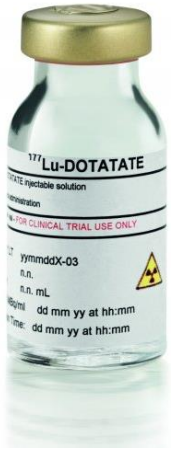
How to progress in the field ?



Courtesy Prof. MD Osman Ratib
in the context of CERN-MEDICIS

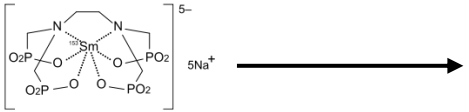
From low to high specific activity radiopharmaceuticals for theranostics

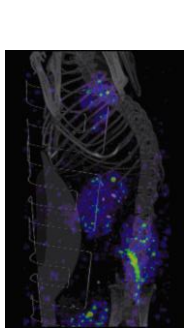
$^{223}RaCl_2$



^{177}Lu-DOTATATE

^{153}Sm-EDTMP
(low specific activity)

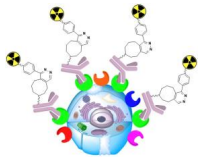




[Production of Sm-153 with high specific activity for targeted radionuclide therapy](#)

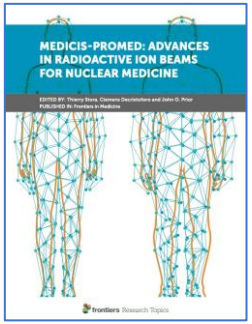
M. van Voorde et al.

^{153}Sm-DOTATATE or other ?

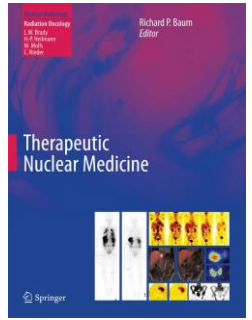


Thank you ! Questions ?

- Some references (highly specialised) :
- Therapeutic nuclear medicine, Richard Baum ed. ISBN: 978-3-540-36719-2
- https://medical-radionuclides.eu
- Frontiers in Medicine : Advances in Radioactive Ion Beams for Nuclear Medicine (J. Prior, C. Decristoforo, T. Stora eds) ISBN 978-2-83250-522-9
- IAEA TecDoc https://www.iaea.org/topics/nuclear-science/isotopes



Helene Langevin-Joliot at MEDICIS, professor in nuclear physics, grand-daughter of Marie Curie



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP).


CERN