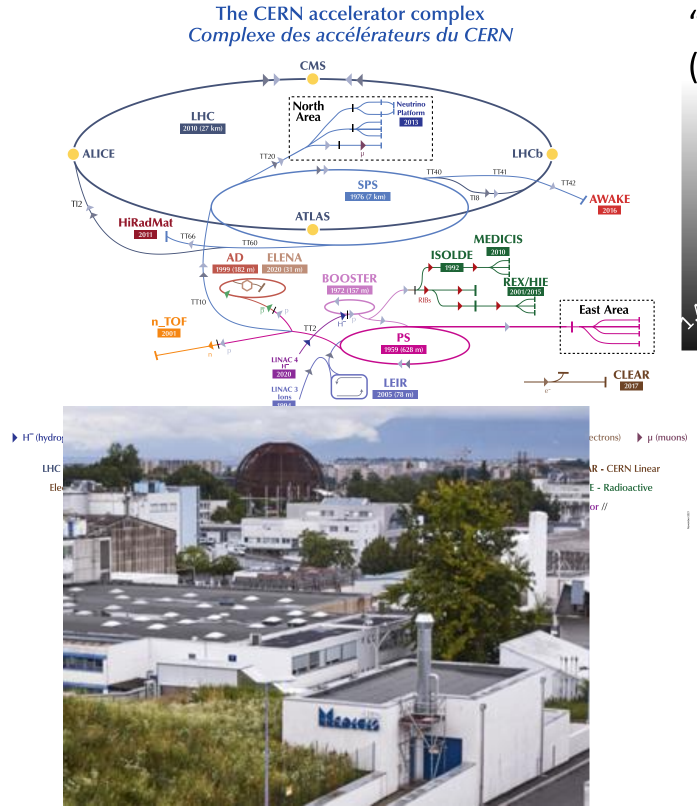
CERN-MEDICIS programme and upgrade plans at ISOLDE

T. Stora

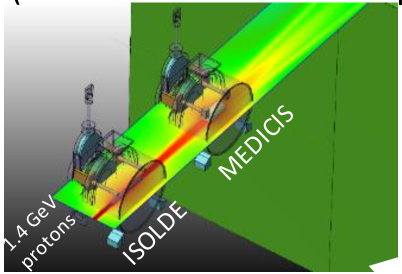
With input/data from A.P. Bernardes, C. Duchemin, M. Fraser, A. Gottberg, S
Marzari, E. Noah, F. Pozzi, J.P. Ramos, S. Stegemann,, S. Rothe, J. Vollaire

1) **Define some unique, desirable radioisotopes that can be produced using high-energy protons incident upon various spallation targets.**
2) **Determine how we can effectively isolate/separate the desired radionuclide(s).**
   a) On-line mass separation?
   b) Bulk post-irradiation chemical and mass separation?
3) **Identify the most challenging technological implementations and roadblocks.**
   a) What are the target technology limitations?
   b) What is the target technical readiness?
   c) What target materials would be interesting in terms of production with either protons or neutrons and post-irradiation handling?
4) **Consider the regulatory aspects/challenges of adding isotope production to a facility (SNS) regulated by the Accelerator order.**

Mass separation as applied in MEDICIS (batch mode) in a snapshot

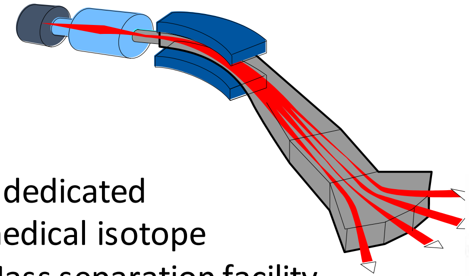


“Free” proton beam
(otherwise lost in the dump)

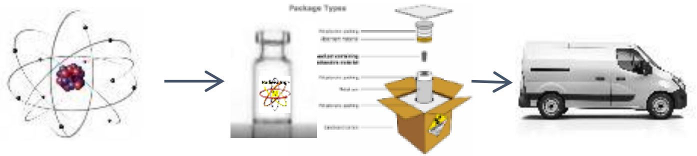


Some **MEDICIS isotopes** :

High activity Sm-153, Ba/Cs-128, Tm/Er-165



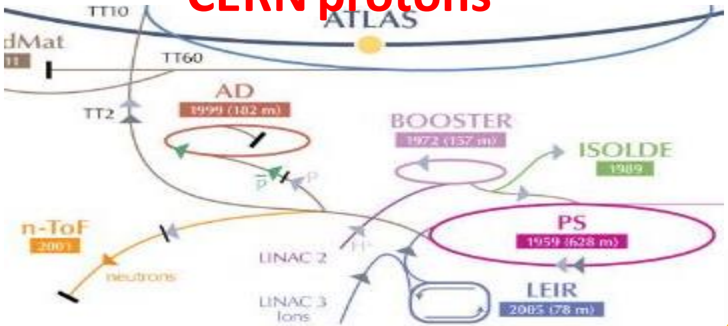
A dedicated medical isotope Mass separation facility in Europe.



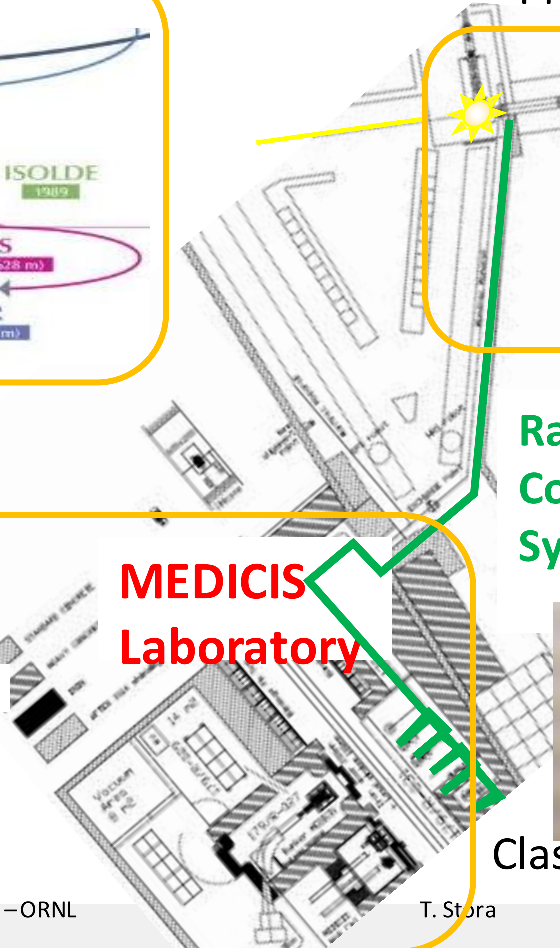
From CERN- MEDICIS to the lab/Hospital

Principle of isotope production

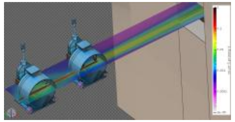
CERN protons

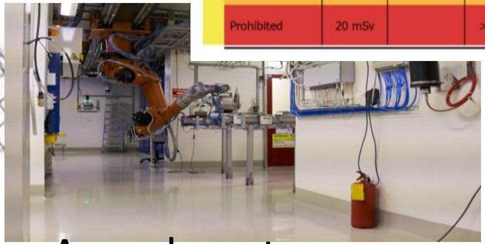


Primary target area



MEDICIS Target Irradiation





Rail Conveyor System

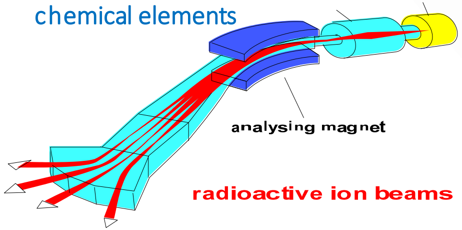
Area	Dose limit [year]	Ambient dose equivalent rate: Work place	Ambient dose equivalent rate: Low occupancy	Sign
Non-designated	1 mSv	0.5 µSv/h	2.5 µSv/h	
Supervised	6 mSv	3 µSv/h	15 µSv/h	
Simple	20 mSv	10 µSv/h	50 µSv/h	
Limited Stay	20 mSv		2 mSv/h	LIMITED STAY SÉJOUR LIMITÉ
High Radiation	20 mSv		100 mSv/h	HIGH RADIATION HAUTE RADIATION
Prohibited	20 mSv		> 100 mSv/h	PROHIBITED AREA ZONE INTERDITE

Radiation Area

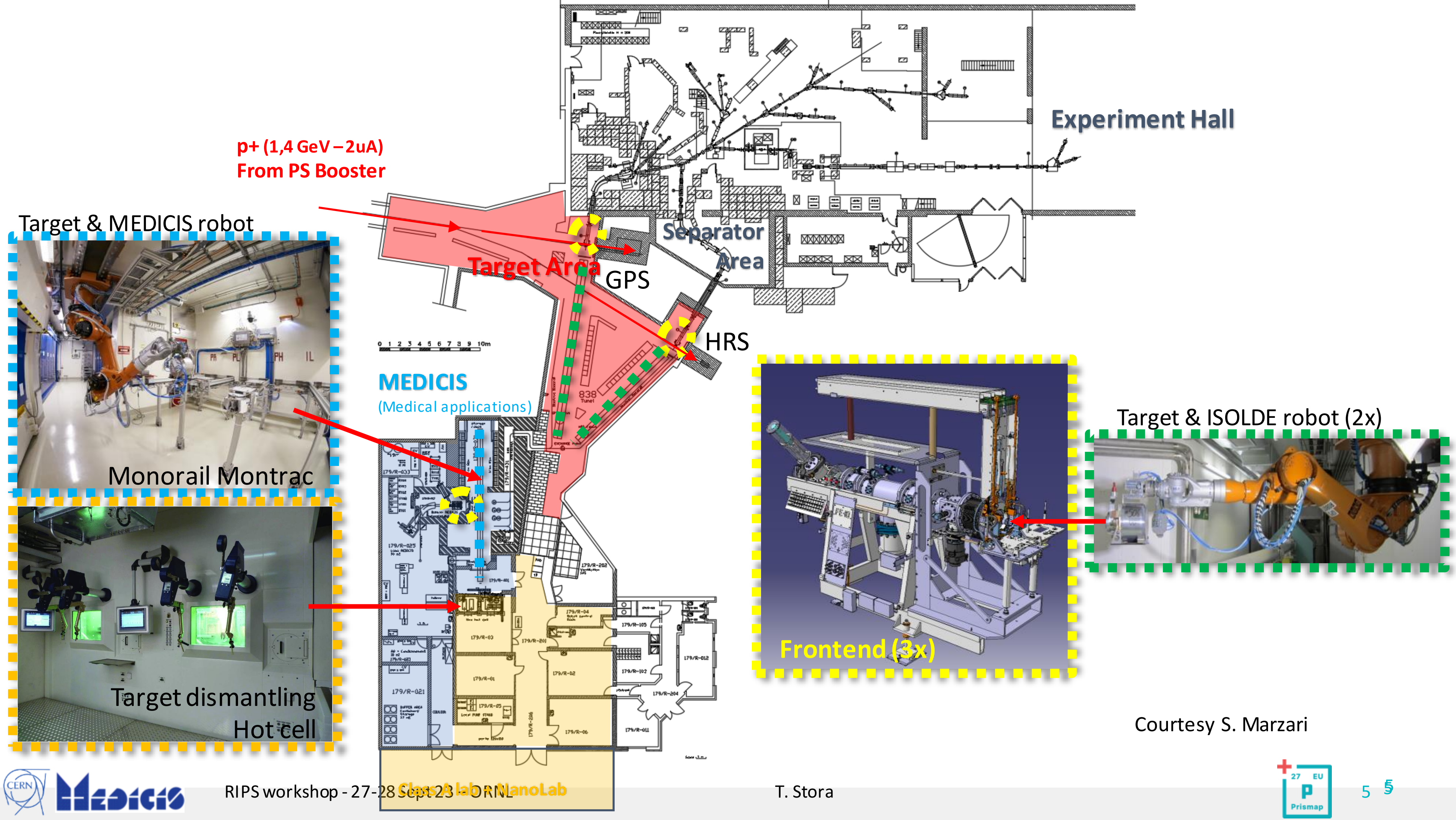
Controlled Area

MEDICIS Laboratory

1000+ isotopes of 70+ chemical elements



Class A work sector


Experiment Hall
p+ (1,4 GeV – 2uA)
From PS Booster
Target & MEDICIS robot
Separator
Area
Target Area
GPS
HRS
MEDICIS
(Medical applications)
Monorail Montrac
Target & ISOLDE robot (2x)
Frontend (3x)
Target dismantling
Hot cell
Class A lab + NanoLab
Courtesy S. Marzari

From excitation function to production rate to source activity to KPI (see later)

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

10^{10}pps   100μA (6.10^{14}) 1mbarn $1 g/cm^2$ for A_{target}=30g/mol

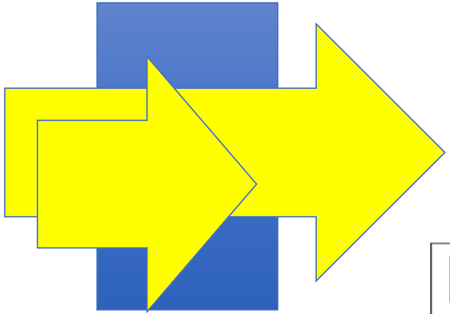
$R\ [Bq] = I\lambda/(1-\lambda) = I$ for 5 $T_{1/2}$ ($\lambda=0.606/T_{1/2}$) **saturation activity**

Incident particle
Beam intensity

$$Y(E_{\text{in}}) = \frac{N_A}{A_T}\int_0^{E_{\text{in}}} \sigma(E)\,\frac{1}{S(E)}\,dE,$$

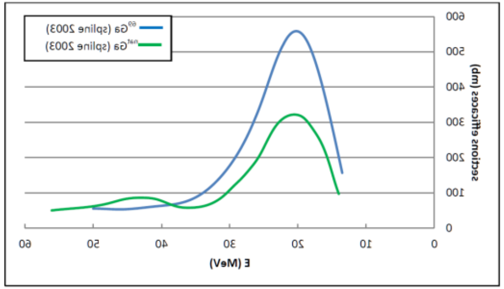
An individual dose

For imaging is ~100 MBq
For treatment ~ 1 GBq
For alpha-therapy ~ 10 MBq

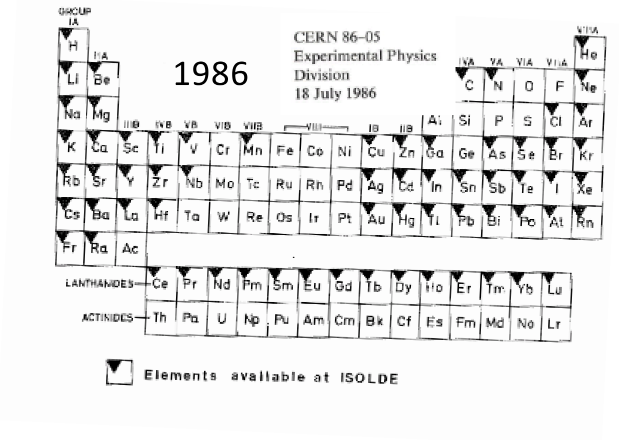


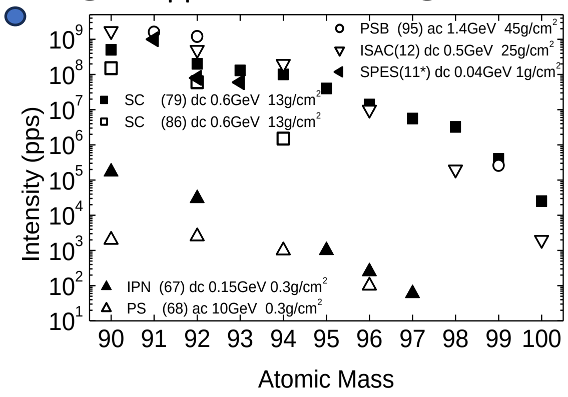
Target thickness

Bragg peak possibly in a dump

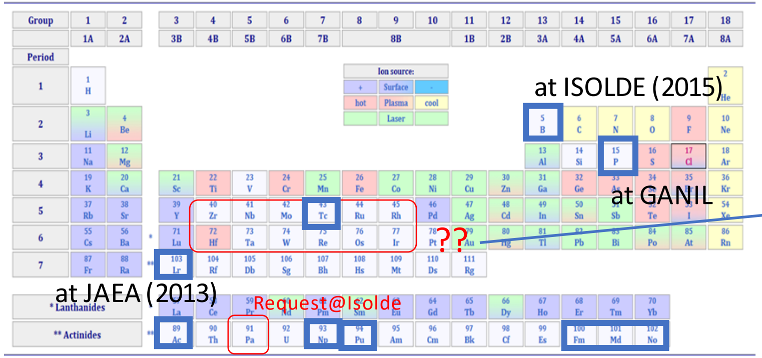


History of isotope beams by mass separation (Online, ISOL)



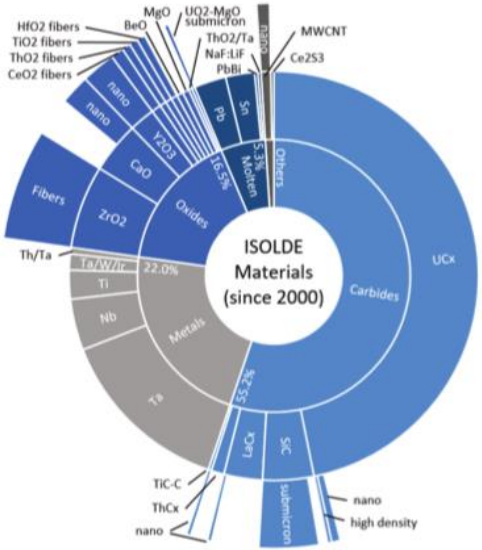


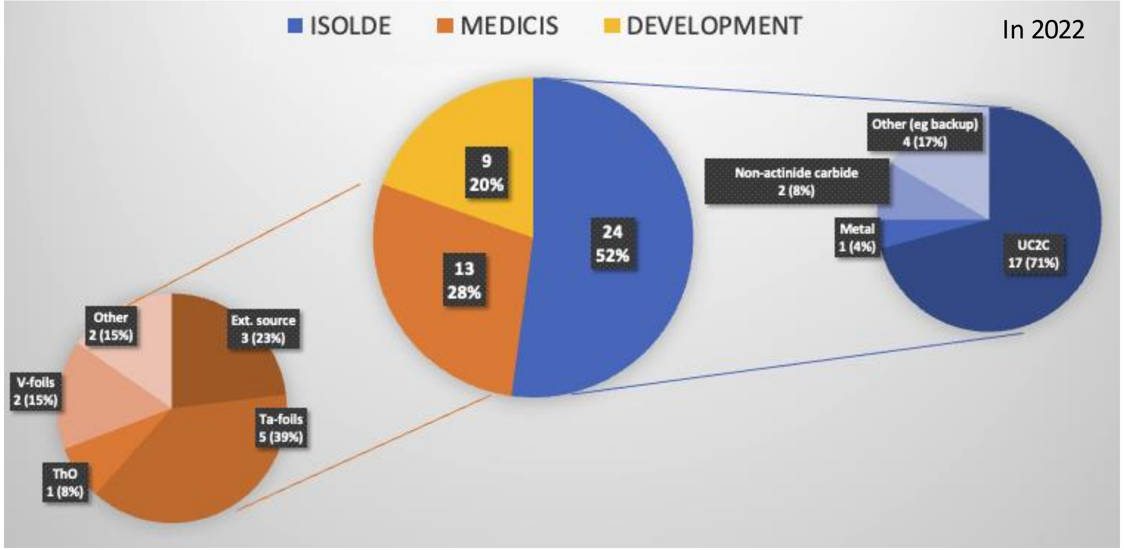
2012 And more recently



We don't easily evaporate/release refractory elements (eg Ac radionuclides)

Target materials in ISOL facilities





J. P. Ramos, https://doi.org/10.1016/j.nimb.2019.05.045 Courtesy S. Stegemann

Target materials in ISOL facilities

120 Materials (possibly more) were tested and/or used as ISOL targets!

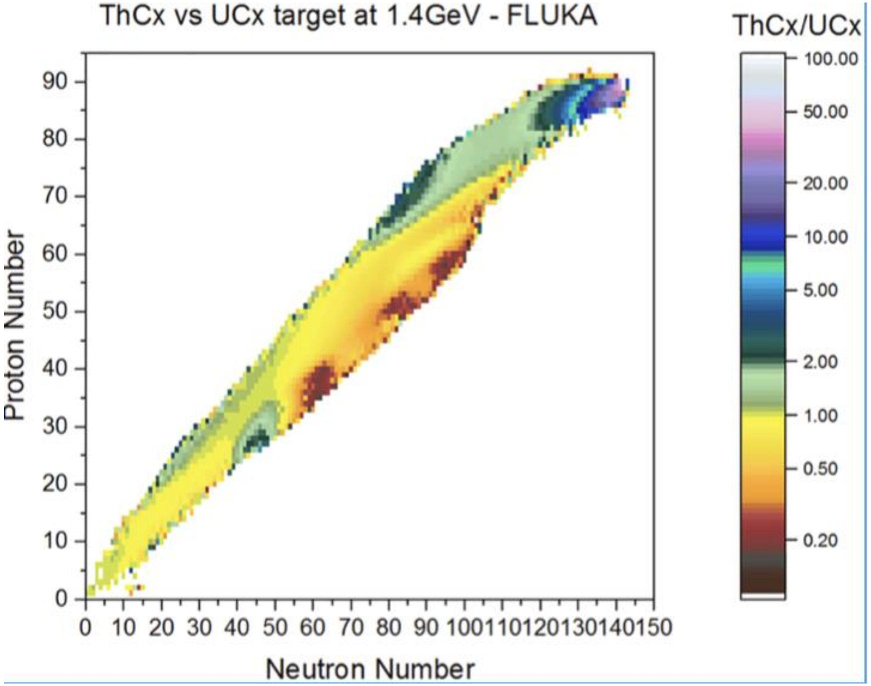
							Oxides				
Carbon Based	AlC_2	B_4C	C(gr)	**C (MWCNT)**	CaC_2	CmC_x	**Al_2O_3**	B_2O_3	BaO	**BeO**	
	GdC_x	**LaC_2**	ScC_2	**SiC**	TaC_x	ThC_2	**CaO**	CeO_2	Cr_2O_3	**HfO_2**	
	TiC	**UC_2**	VC	ZrC	Cm	Hf	La_2O_3	MgO	**NiO**	SrO	
	Ir	Ir/C	Ta/Ir/W	Mo	Nb	Os	Ta_2O_3	**ThO_2**	**TiO_2**	UO_2	
	Pu	Pt/C	Re	Re/C	Ru	Ru/C	Si layers	**Y_2O_3**	**ZrO_2**	ThO2/Ta	
Solid Metals	Sn/C	**Ta**	Ta/W	Ti	Th	Th/Ta	AlN	BaB_6	$BaZrO_3$	$TiO_2.(H_2O)_x$	**First Materials**
	Th/Nb	U	U/C	V	W	Zr	BN	Ca-zeolite	CaB_6	$ZrO_2.(H_2O)_x$	
	Au	Ag	Bi	Cd	Ce	Ce_3S_4	$Ce(OH)_4$	CaF_2	CeB_6	$CeO_2.(H_2O)_x$	
	Er:Cu	Ge	Gd:Cu	Hg	La	La:(Th/Si/Sc)	CeS	LuF_3	Na-zeolite	$ThO_2.(H_2O)_x$	
	La:(Y,Gd,Lu)	**NaF:LiF**	$NaF:ZrF_4$	Nd	Ni	Pr	Ta_5Si_3	Hf_5Ge_3	Hf_5Si_3	Sr stearate	
	Pt:B	Sc:La	Sn	Tb	$TeO_2:KCl:LiCl$	$ThF_4:LiF$	Hf_5Sn_3	Ta_5Si_3	Tl-zeolite	Ba stearate	
	Pb	**Pb:Bi**	Y:La	U	U:Cr	Zn	$Th(OH)_4$	Zr_5Ge_3	Zr_5Si_3	$TeCl_4$	
	Molten						**Others**				

J.P. Ramos, PhD Thesis, EPFL/CERN (2017)

- In squares – currently used at ISOLDE
- **Underlined and Bold** – had been subject of material development

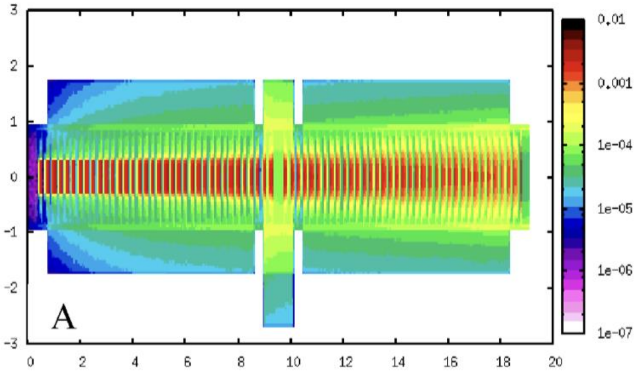
Which target, which beam characteristics

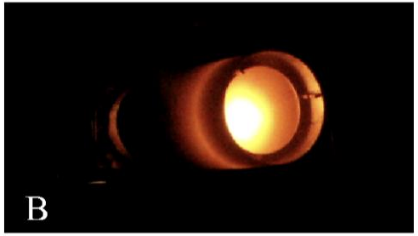
Ratio of production



J. P. Ramos, https://doi.org/10.1016/j.nimb.2019.05.045

Al_2O_3-Nb 25kW ISOL target

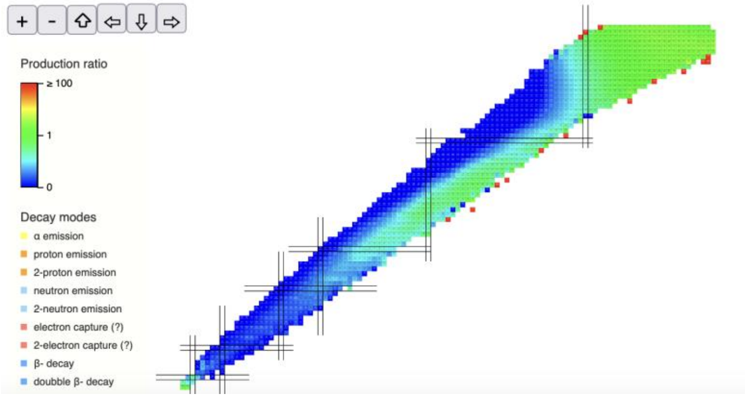




T. Stora et al, EURISOL-DS (100kW 1 GeV oxide targets)
https://doi.org/10.1063/1.3120150

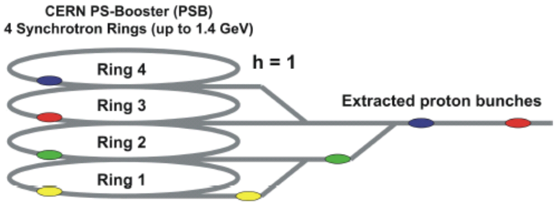
Specificity of a PSB pulsed beam at CERN : high energy, pulsed beam

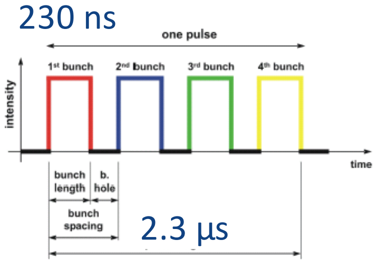
Comparison of 0.5 to 2 GeV : Ta roll target



https://isoyields2.web.cern.ch/InTargetProductionChart.aspx

Beam power deposition – pulsed beams!

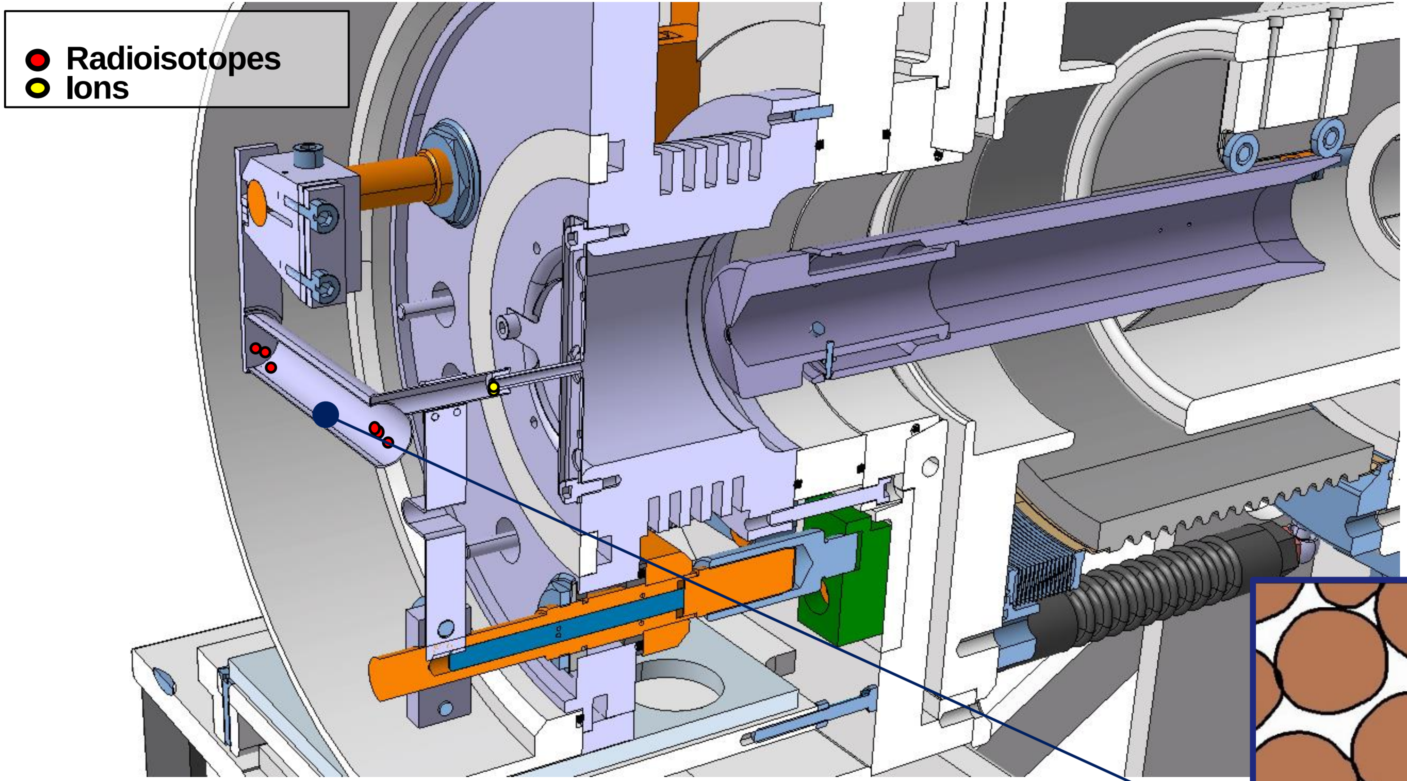




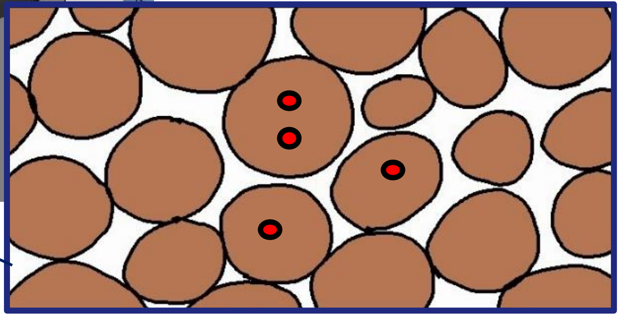
Thermomechanical stresses and shockwaves

Beam power
- 2.8 kW in average
- 1.2 GW (pulse length 2.3 µs)
  - ~10% deposited

→ ISOLDE upgrade(s) programme : higher intensity, 1.4-2GeV

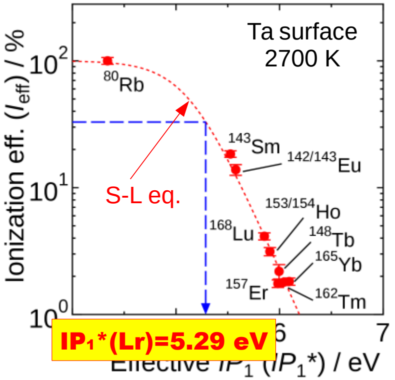


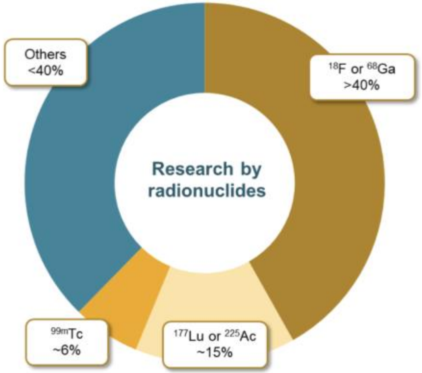
Standard ISOLDE target unit with ***surface (or laser)*** *ion source*



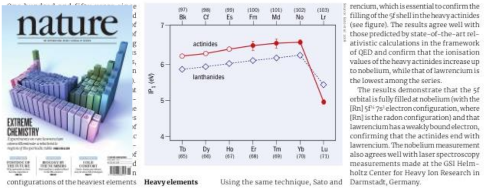
Raciochemical process(es) of the targets prior or after in the MEDICIS or external laboratories

Fom one-atom-at-a-time experiments to large production needs





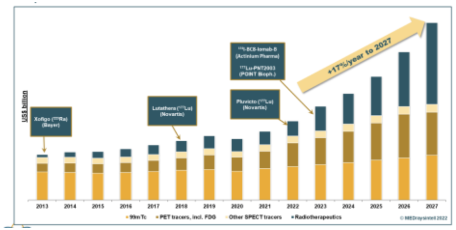
MEDraysintell


NEWS ANALYSIS

PERIODIC TABLE

Actinide series shown to end with lawrencium

Heavy elements



Ionisation efficiencies

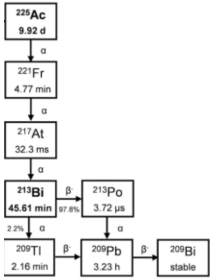
^{153}Sm	12.7
^{167}Tm	55 %
^{155}Tb	1-6
^{225}Ac	15.1 %

Johnson, J.D., et al. Sc. Rep.13, 1347 (2023)

$^{223-225}$Ra 30-45%*,

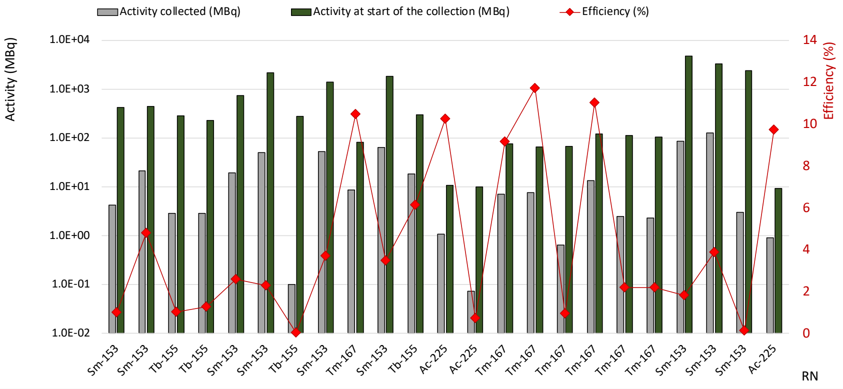
*C. Duchemin et al.

strategies to double this figure already initiated



Introduction of Key Performance Indicators at MEDICIS

- **KPI 1 : Efficiency and Activity (0.1-100% / kBq-GBq) (→ luminosity)**
- **KPI 2 : Dosimetry (uSv / contamination / events)**
- **KPI 3 : Importance (high/medium/low) (→ reliability)**
- **KPI 4 : Timing (T process, import/export vs T1/2 isotope) (→ downtime)**



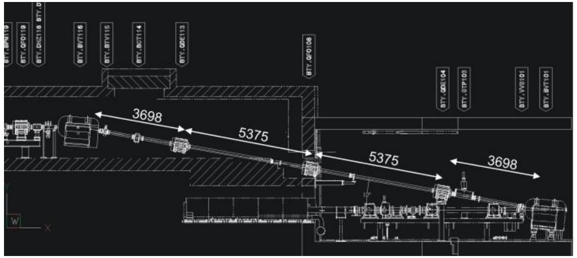
In these 4 KPIs are hidden some others, eg down-time / up-time of the facility, delivered poT and useful proton on MEDICIS target, mode of failure, planning, …

IPAC

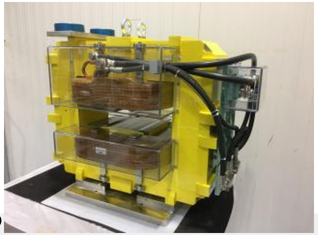
Upgrade of the proton beam line (BTY line)*

- PS Booster energy increase in 2020 (1.4 GeV to 2.0 GeV) as part of the LIU project (LHC injectors upgrade)
- Reconfiguration of the BTY line (beam line to ISOLDE) planned in 2025 in parallel to the Power Converters replacement to benefit from the 2.0 GeV beam (increased production yields for several radionuclides). 1.4 GeV kept as operational beam.
- Geometrical reconfiguration of the vertical dogleg between the PS Booster and ISOLDE and addition of two dipoles for the HRS target station switch. Detailed optics and integration studies ongoing.

New design for the vertical dogleg
(same dipole changing the angle)



HRS switch (horizontal)



Current vertical dogleg

CERN | SY Accelerator Systems

REFERENCE
PSB-RP-ES-0002

Date: 2023-07-05

FUNCTIONAL SPECIFICATION

Sirius S and 2P Power Converters for Magnets of the PSB-BTY Transfer Line in the Framework of the Accelerator Consolidation Project

ABSTRACT:

This document covers the functional specifications of SIRIUS converters for the replacement of old power supplies in the framework of the accelerator consolidation program for the PSB-BTY Transfer line.

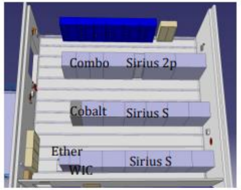


Figure 7 — Building 197/1-401: possible integration of SIRIUS converters.

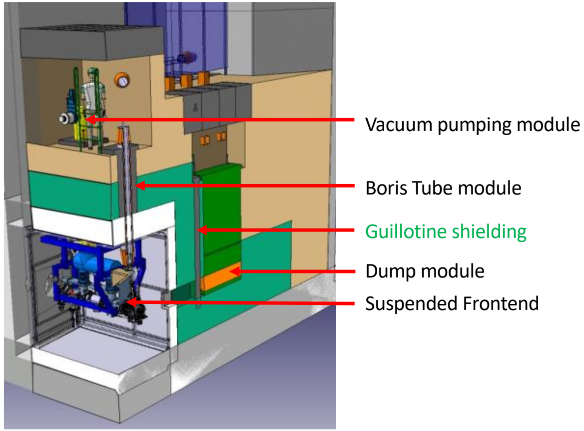
* Full consolidation programme under prioritization

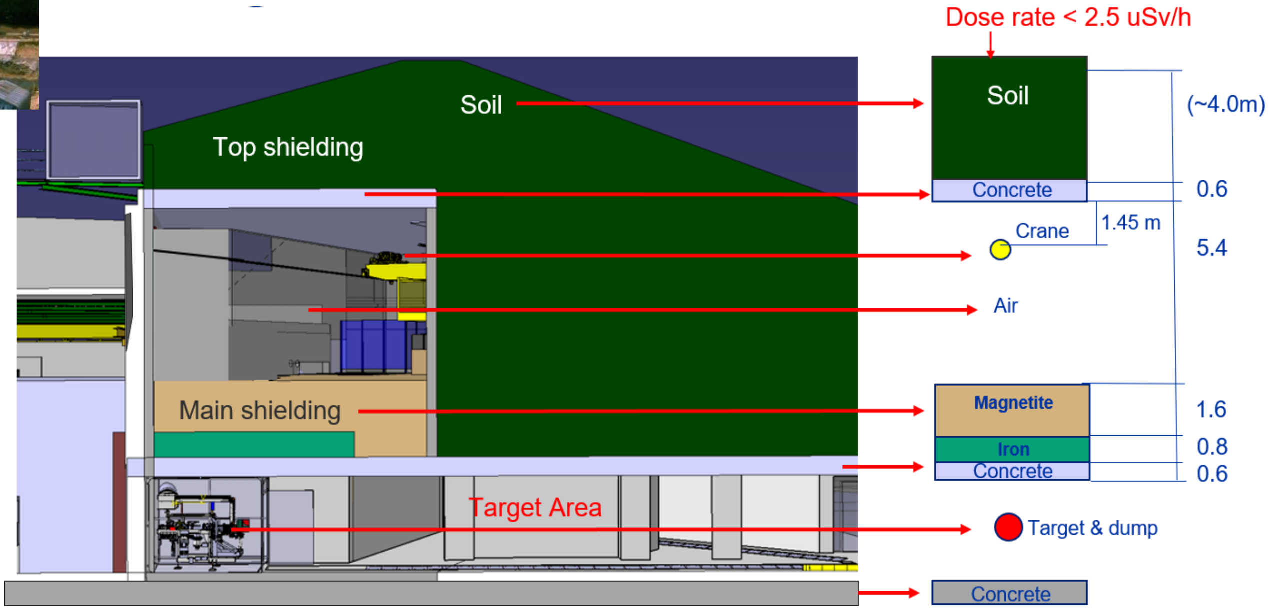
Courtesy M. Fraser, J. Vollaire

Options for Front End and target area upgrades (Beam Dump Replacement)*

Commissioning of new :
building, crane, shielding, dumps, guillotine shielding

Upgrade => New Frontend design





- Full consolidation programme under staging and prioritization

Courtesy A.P. Bernardes, S. Marzari

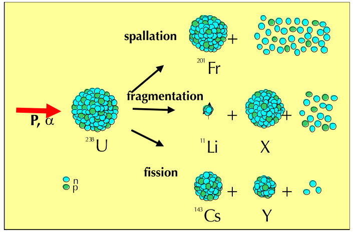
How to supply "novel" radionuclides with mass separation

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

Accelerator

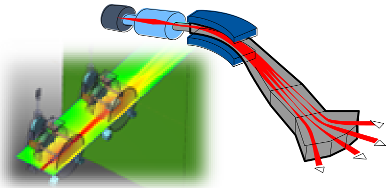
Isotope mass separation

Research reactor

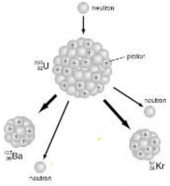


$I_{[pps]} \sim F_{[pps]}\ S_{[barn]}\ N_{[g/cm2]}$ **production rate**

10^{10}pps 100µA (6.10^{14}) 1mbarn 1g/cm^2 for A_{target}=30g/mol



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

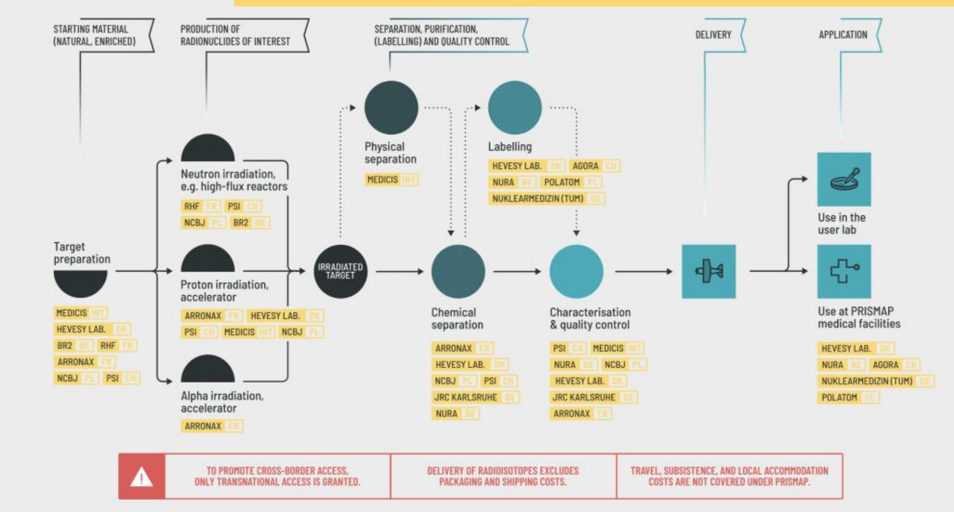


$$\frac{dN'}{dt} = n v \sigma_{act} N_T$$

target transfer
into Isotope mass separation unit

PRISMAP.EU

- Our web interface : https://www.prismap.eu/radionuclides/portfolio/



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

Translation : Regulation of radiopharmaceuticals : Swiss example

swissmedic

Fabrication :
Used nuclear reaction - isotope halflife
Radiation type and energy
Pertubation induced by impurities

Nuclides produced by target irradiation
Target material, target envelop
Composition, chemical form, purity, physical state,
Chemical additives, capable to impact the end product
Irradiation method, physical and chemical environment
Target support
Yield

Nuclide treatment
- Description of isolation (separation from the target), nuclide concentration, yield.

Physical properties of nuclides
In detail : halflife, type and energy of radiation, evolution over time from the fabrication to the date of peremption of the drug, important aspects for disposal

Nuclides from fission
Full nuclide reaction chain, initial material (including impurities), daughter nuclides, halflifes, radiation type and energy
Pertubation from impurities

End product control
- Nuclide identity
- Purity of nuclides
- Radiochemical purity
- Chemical purity
- Specific activity

Ident. QM : ZL000_00_003f_WL / V01 / bg, stb, cas / zro / 01.04.2015

- Thank you !

- Some more info connected to the RISP-ORNL project:
- eg EURISOL-DS 100kW direct targets (1GeV cw beam baseline) technical reports, and eventual follow-up projects
- MEDICIS-promed: Advances in radioactive ion beams for nuclear medicine. *Frontiers in medicine*, *9*, 1013619. (Topical volume)
- Medicis.cern
- prismap.eu websites

CERN

Some yield estimates

Medical pplication	Isotope half-life	Parent isotope beam	Target - Ion source	ISOLDE† In-target Production rate (pps)	ISOLDE† In-target ActivityEOB (Bq)	RIB Ɛext** (%)	CERN-MEDICIS† In-target ActivityEOB (Bq)	CERN-MEDICIS† Extracted Activity EOB (Bq)	CERN-MEDICIS 2GeV 6µA Possible gain Ɛext (%)	CERN-MEDICIS 2GeV 6µA In-target Activity EOB/	Extracted Activity EOB (Bq)	Comments
3- therapy/ :T/dosimetry	^{213}Bi 45.6m	^{225}Ac	UCX-Re	1.5E9*	7.2E8	^{221}Fr 10	2.8E8	2.8E7	50	8.4E8	4.2E8	Only mass separation
.β therapy	^{212}Bi 60.6m	^{224}Ac	UCX-Re	1.5E9*	1.4E9	^{220}Fr 10	1.7E9	1.7E8	50	5.1E9	2.5E9	Only mass separation
β therapy	*^{177}Lu 6.7d*	*^{177}Lu RILIS/VD*	*Ta-Re/ Re-VD5*	*3.3E9*	*7.4E8*	*^{177}Lu 1*	*6.4E8*	*6.4E6*	*20*	*8.3E8*	*1.7E8*	*Chemical purification*
ger therapy	^{166}Yb 56.7h	^{166}Yb	Ta-Re	1.4E10	5.4E10	^{166}Yb 5	4.1E10	2.1E9	20	5.4E10	1.1E10	Chemical purification
β therapy	*^{166}Ho 25.8h*	*^{166}Ho*	*Ta-Re*	*1.4E7*	*1.2E7*	*^{166}Ho 5*	*9.6E6*	*4.8E5*	20	*2.9E7*	*6.0E6*	Chemical purification
uger therapy	*^{161}Tb 6.9d*	*^{161}Tb*	*UCX-Re*	*2.1E7*	*2.7E7*	*^{161}Tb 5*	*1.9E7*	*9.5E5*	20	*2.7E7*	*5.4E6*	Chemical purification
3- therapy	*^{156}Tb 5.35d*	*^{156}Tb*	*Ta-Re*	*2.5E8*	*8.9E7*	*^{156}Tb 1*	*5.5E7*	*5.5E5*	*20*	*6.3E7*	*1.3E7*	Chemical purification
SPECT	^{155}Tb 5.33d	^{155}Dy/ Tb	Ta-Re	3.2E9/ 7.4E8	7.9E9	^{155}Dy 1	5.3E9	5.3E7	20	3.4E9	6.8E8	RILIS Dy
3 therapy	^{153}Sm 46.8h	^{153}Sm	UCX-Re	1.5E8	2.2E9	^{153}Sm 5	2.8E9	1.4E8	20	5.2E9	1.0E9	Chemical purification
PET/CT	^{152}Tb 17.5h	^{152}Dy/ Tb	Ta-Re	1.3E10/ 3.3E9	5.6E10	^{152}Dy 1	3.7E10	3.7E8	20	1.1E11	2.2E10	RILIS Dy
ι therapy	^{149}Tb 4.1h	^{149}Tb	Ta-Re	1.1E10	6.0E10	^{149}Tb 1	3.8E10	3.8E8	20	1.2E11	2.4E10	Chemical purification

^{40}Pr-PET/ ger therapy	^{140}Nd 3.4d	^{140}Nd	Ta-Re	1.8E9	2.0E10	^{140}Nd 5	1.2E10	6.0E8	20	2.0E10	4.0E9	Chemical purification
- therapy	^{89}Sr 50.5d	^{89}Sr	UCX-Re	1.2E10	2.3E9	^{89}Sr 5	2.0E9	1.0E8	20	2.7E9	5.4E8	Only mass searation
PET	^{82}Sr 25.5d	^{82}Sr	UCX-Re	3.6E10	4.6E9	^{82}Sr 5	1.7E9	8.5E7	20	2.0E9	4.0E8	Only mass separation
- therapy	^{77}As 38.8h	^{77}As	UCX-VD5	5.7E9	1.1E10	^{77}As 5	5.8E9	2.9E8	20	9.4E9	1.4E9	Chemical purification
PET	^{74}As 17.8d	^{74}As	Y_2O_3 -VD5	6.5E9	1.2E9	^{74}As 5	3.8E8	1.9E7	20	4.5E8	9.0E7	Chemical purif
PET	^{72}As 26.0d	^{72}As	Y_2O_3 -VD5	1.6E10	2.8E10	^{72}As 5	9.1E9	4.6E8	20	1.5E10	3.0E9	Chemical purification
PET	^{71}As 65.3h	^{71}As	Y_2O_3 -VD5	1.8E10	1.8E10	^{71}As 5	5.9E9	3.0E8	20	8.0E9	1.6E9	Chemical purification
3 therapy	^{67}Cu 61.9h	^{67}Cu	UCX-Re	2.7E9	3.4E9	^{67}Cu 7	1.5E9	1.1E8	20	2.7E9	5.4E8	Chemical purification
PET	^{64}Cu 12.7h	^{64}Cu	Y_2O_3 -VD5	1.1E10	2.3E10	^{64}Cu 5	7.1E9	3.6E8	20	2.1E10	3.6E9	Chemical purification
, dosimetry	^{61}Cu 3.3h	^{61}Cu	Y_2O_3 -VD5	7.7E9	1.7E10	^{61}Cu 5	5.1E9	2.6E8	20	2.1E10	4.0E9	Only mass separation
3 therapy	^{47}Sc 3.4d	^{47}Sc	Ti	6.4E10	5.0E10	^{47}Sc 5	4.2E10	2.1E9	20	5.9E10	1.2E10	Evaporation
PET	^{44}Sc 4.0h	^{44}Sc	Ti	4.4E10	6.6E10	^{44}Sc 6.4	5.7E10	2.9E9	20	1.6E11	3.2E10	Evaporation
PET	^{11}C 20.3m	^{11}CO	NaF-LiF-VD5$^{\lozenge}$	-	-	- 15	-	1.4E9	-	-	4.2E9	Only mass separation

The idea in the back of PRISMAP : The European Medical Radionuclide Programme

Element	Z	Isotope	Property / Application	Imaging/Treatment/ Generator	Production ~~reaction~~
Sc	21	44g/m	PET	I	^{44}Ca(p,n) or ^{44}Ca(d,2n)
Sc	21	47	b^- therapy, SPECT	I/T	^{46}Ca(n,g)^{47}Ca(b^-)
Cu	29	64	PET	I	^{64}Ni(p,n) or ^{64}Ni(d,2n)
Cu	29	67	b^- therapy, SPECT	I/T	^{68}Zn(p,2p) or ^{70}Zn(p,a)
Ag	47	111	b^- therapy, SPECT, TDPAC	I/T	^{110}Pd(n,g)^{111}Pd(b^-) or ^{110}Pd(d,n)
La	57	135	Auger emitter	T	^{135}Ba(p,n)- or ^{nat}Ta(p,spall)+mass separation
Tb	65	149	a therapy, PET	I/T	^{nat}Ta(p,spall) +mass separation
Tb	65	152	PET	I	^{nat}Ta(p,spall)+mass separation
Tb	65	155	Auger emitter, SPECT	I	^{nat}Ta(p,spall)+mass separation
Tb	65	161	b^- therapy, SPECT	I/T	^{160}Gd(n,g)b^-
Dy	66	166	Generator for ^{166}Ho (b^-, SPECT)	G	^{164}Dy(n,g)(n,g)
Er	68	165	Auger emitter	T	^{165}Ho(p,n)
Tm	69	165	Generator for ^{165}Er (Auger em.)	G	^{nat}Ta(p,spall)+mass separation
Er	68	169	b^- therapy	T	HSA ^{168}Er(n,g) +mass separation
Yb	70	175	b^- therapy, (SPECT)	T	HSA ^{174}Yb(n,g) +mass separation
Pt	78	195m	Auger emitter, SPECT	I/T	^{194}Pt(n,g)
Bi	83	213	a therapy	T	^{225}Ac generator
At	85	211	a therapy	T	^{209}Bi(a,2n)
Ac	89	225	a therapy	T	^{229}Th generator
Ac	89	225	a therapy	T	^{232}Th(p,spall)+mass separation

A formalized ALARA approach is vital for a successful Radiation Protection of over 10’000 Radiation Workers and is supported and enforced by the CERN management.
Optimization at CERN is consistently implemented from design, operation to dismantling of facilities at various levels depending on the radiological risks

Group 1 criteria define **ALARA level**

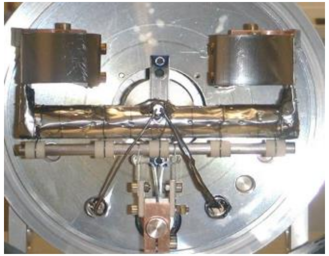
Individual dose equi.	**Level I**	100 µSv	**Level II**	1 mSv	**Level III**
Collective dose equi.		500 µSv		5 mSv	

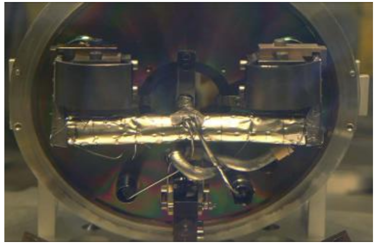
Group 2 criteria are the **bases of a radiological risk assessment** (including accidents and incident scenarios) by the RSO and HSE-RP prior to the final ALARA level classification of the intervention.

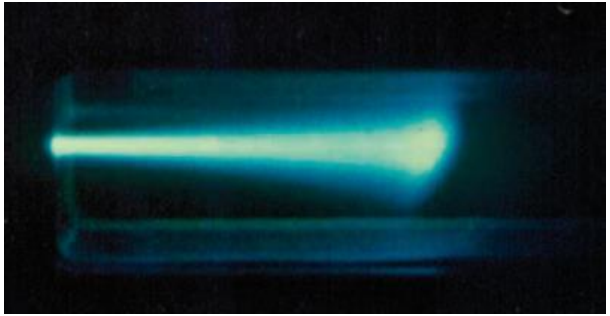
Ambient dose equivalent rate	**Level I**	50 µSv/hr	**Level II**	2 mSv/hr	**Level III**
Airborne activity in CA		5 CA		200 CA	
Surface contamination in CS		10 CS		100 CS	

Operational RP at MEDICIS - Heinz VINCKE

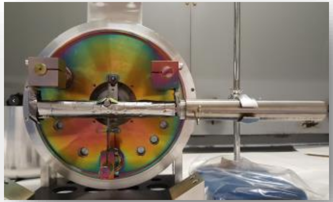
Beam – target interaction and chemical aspects



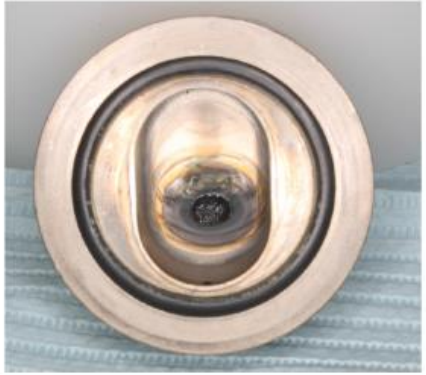




Gas target
(ie N_2 + trace of O_2 for $^{14}N(p,\alpha)^{11}CO_2$)



Cyclotron target transfer
into Isotope mass separation unit



M. Stokely, BTI Targetry

https://youtu.be/p3sjf7ZMPZQ

http://isotopes.lanl.gov/