CERN MEDICIS facility for the production of medical research isotopes…
et plus si affinité

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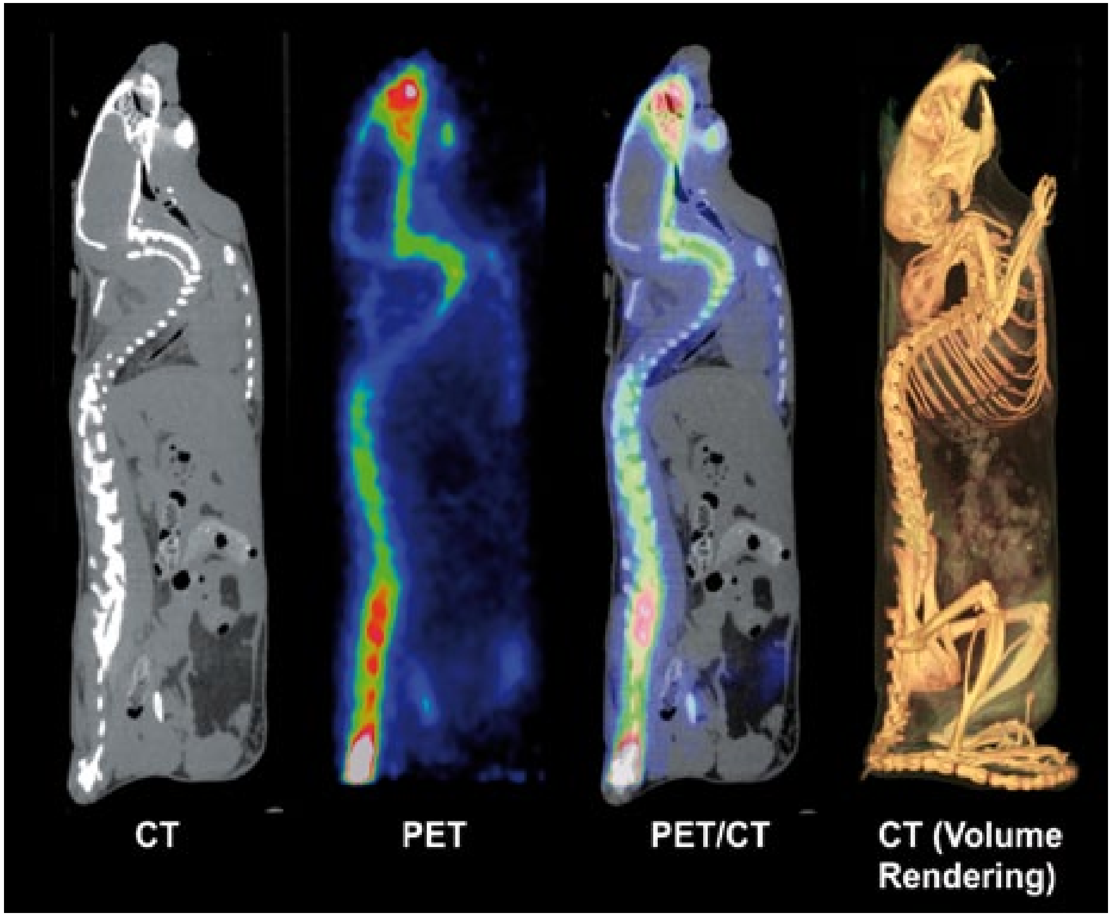
- Novel medical radioisotopes from ISOLDE
- CERN MEDICIS
- Exploring new opportunities



Research on novel medical radioisotopes from ISOLDE

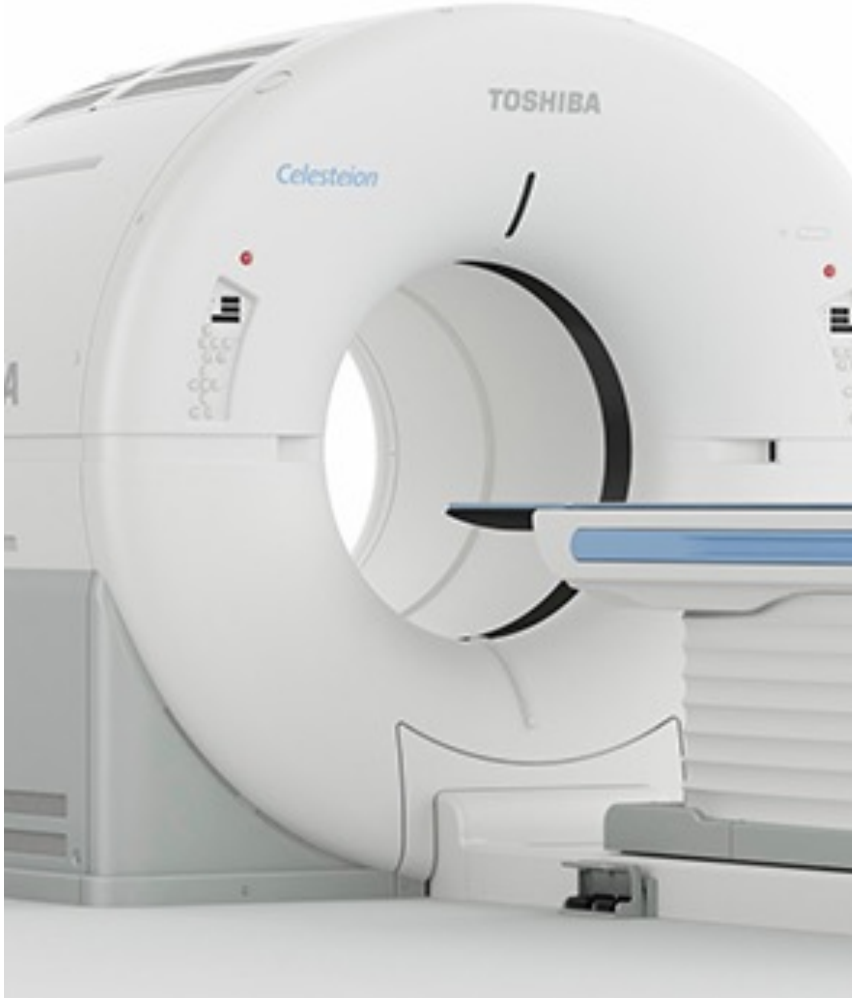
Nuclear vs Radiation Medicine

Radiation Medicine

- ✦ External source (e.g. gamma rays, protons)
- ✦ Non invasive
- ✦ Tuneable

- Accuracy affected by patient's motion
- Induces damage on its path
- Limited to local targets (e.g. tumour)

Nuclear vs Radiation Medicine



Nuclear Medicine

- ✦ Targeted
- ✦ Whole-body coverage
- ✦ Avoids healthy cells

- Requires bespoke research for each case
- Kidney / liver intake
- Prolonged exposure passed the treatment

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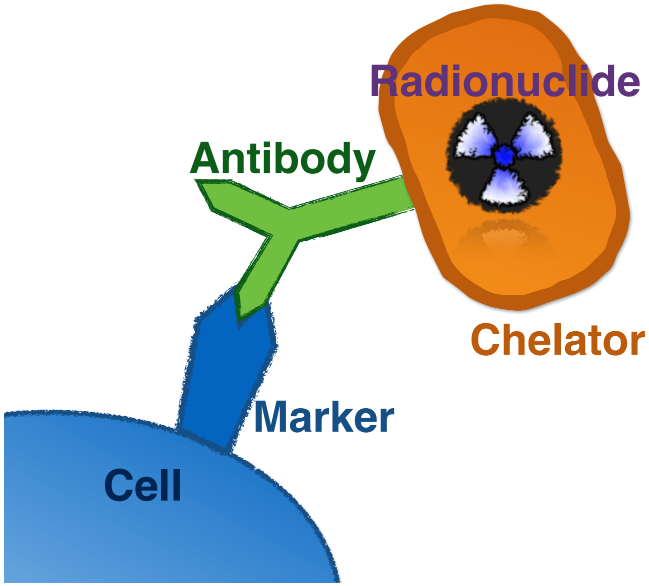
Radioisotopes for nuclear medicine

Radioisotopes are attached to biomolecules used to target specific receptors in the body to image active areas, identify cells, or treat cancer.

Medical radioisotopes have to answer many criteria:
- ➡ available (production)
- ➡ can be handled (half-life)
- ➡ high benefit / low toxicity (decay modes, branching ratios, half-life, purity)
- ➡ stable within the biomolecule

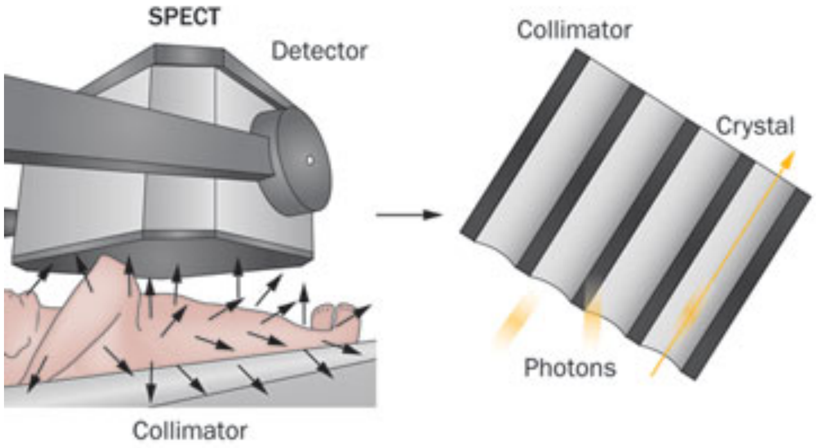


Imaging in Nuclear Medicine

SPECT

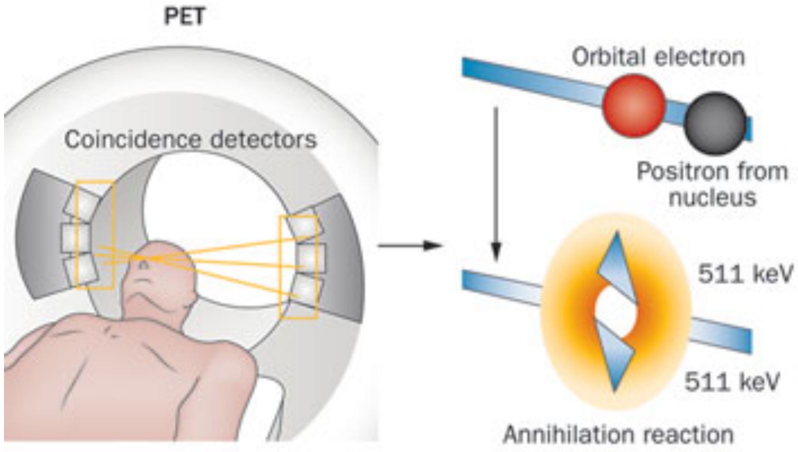
Single Photon Emission
Computed Tomography

- Low-energy gamma ray spectroscopy
- Pb mask to guide orthogonal rays only
- Gantry rotating around the patient to reconstruct 3D image



Typical isotope: ^{99m}Tc

Imaging in Nuclear Medicine



PET

Positron Emission Tomography

- Positron annihilation yields two gamma rays at 511 keV and opposite directions
- Scintillators on opposite sides provide line to interaction point
- Time difference allows to complete the 3D reconstruction

Typical isotope: ^{18}F

Imaging in Nuclear Medicine

SPECT

Single Photon Emission Computed Tomography

- Low-energy gamma ray spectroscopy
- Pb mask to guide orthogonal rays only
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PET

Positron Emission Tomography

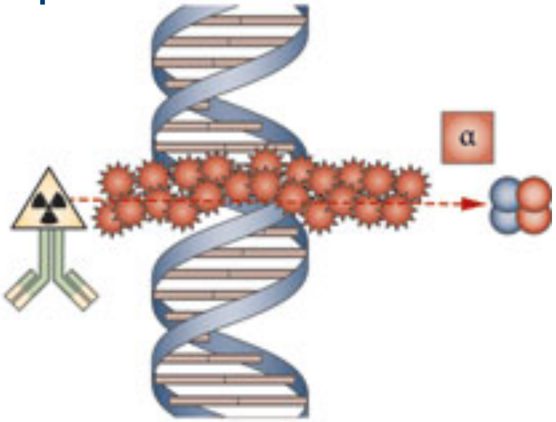
- Positron annihilation yields two gamma rays at 511 keV and opposite directions
- Scintillators on opposite sides provide line to interaction point
- Time difference allows to complete the 3D reconstruction

Treatment in Nuclear Medicine

Alpha therapy

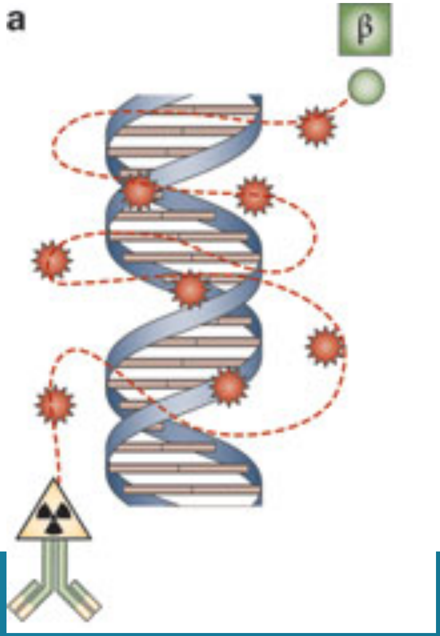
- Short range
- Large damage
- Recoils break free from molecules
- Dangerous to manipulate

Typical isotope:
^{223}Ra



Beta therapy

- Range up to mm
- Partial energy deposition requires higher dose for damage
- Locked in the biomolecule
- Easy to manipulate

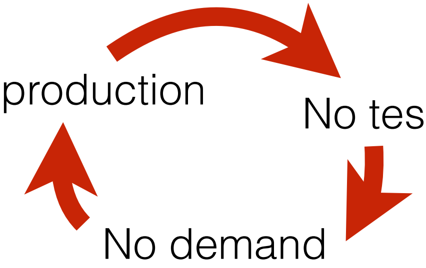


Typical isotope:
^{131}I

Radioisotopes for nuclear medicine

Most of the radioisotopes used nowadays in nuclear medicine are produced in research reactors (e.g. BR2 in SCK•CEN, Mol, Belgium) or at cyclotron facilities directly on the hospital site.

The choice of radioisotopes is limited to a handful — amongst the 3,000 radioisotopes known across the nuclear landscape — mostly due to a source & demand conundrum.



No production

No test

No demand

BR2 reactor at SCK•CEN, Mol

Theranostics: a new concept

To best adapt the treatments to each patient, it is essential to be able to diagnose their condition accurately and to know the treatment reflects the diagnosis.

By using different isotopes of the same element, the distribution of the active agent can be accurately understood to optimise the treatment and minimise the negative impact of the exposure to radiation.

Tb 149		Tb 152		Tb 155	Tb 161
4.2 m	4.1 h	4.2 m	17.5 h	5.32 d	6.90 d
ϵ β^+ α 3.99 γ 796; 165…	ϵ α 3.97 β^+ 1.8 γ 352; 165…	Iγ 283; 160… ϵ; β^+… γ 344; 411…	ϵ β^+ 2.8… γ 344; 586; 271…	ϵ γ 87; 105;… 180, 262	β^- 0.5; 0.6… γ 26; 49; 75… e^-

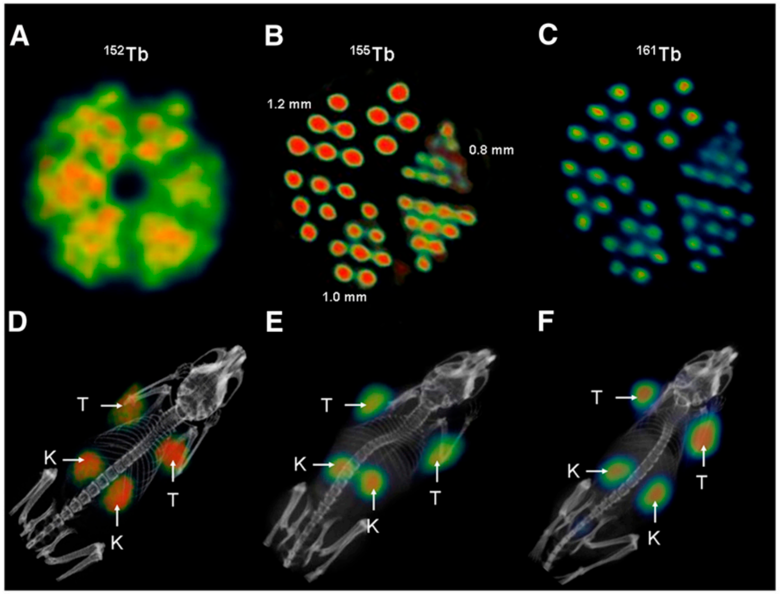
Existing knowledge

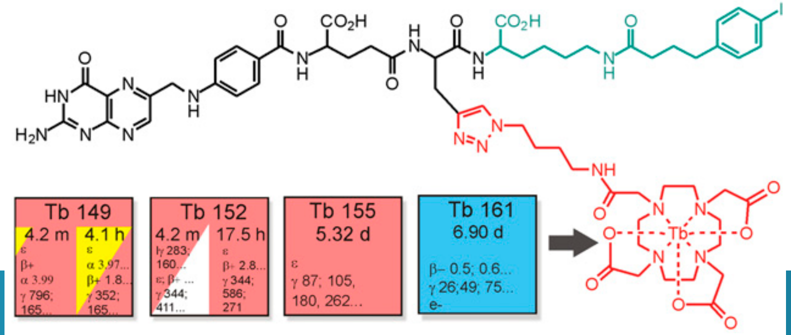
Tb in the Pharmacopeia

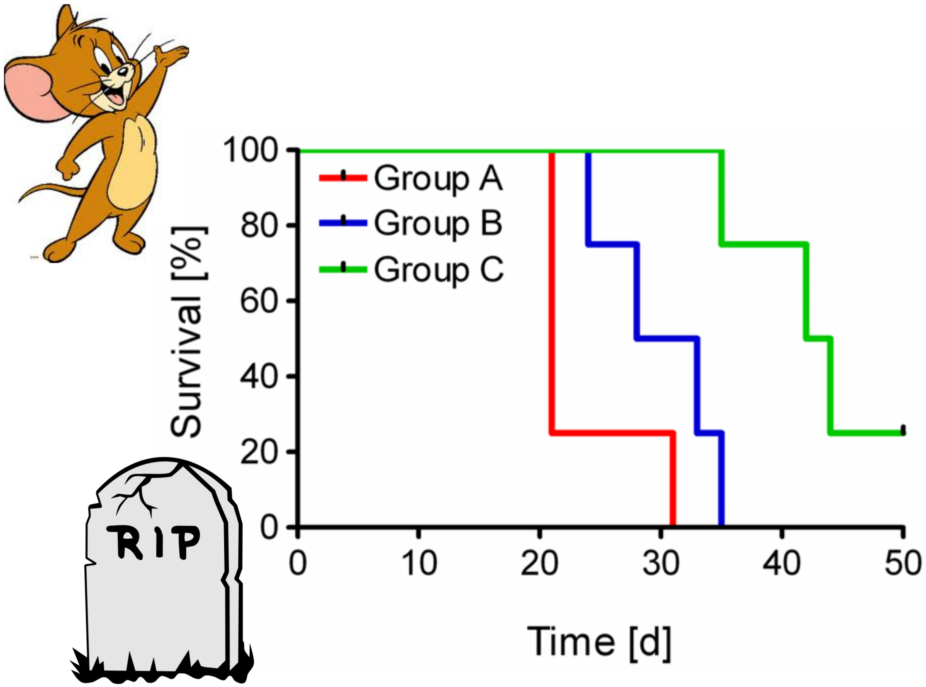
— insert information here —

Tb from ISOLDE to PSI

Tb collection are performed twice a year and shipped within the day to the Paul Scherrer Institute in Villigen



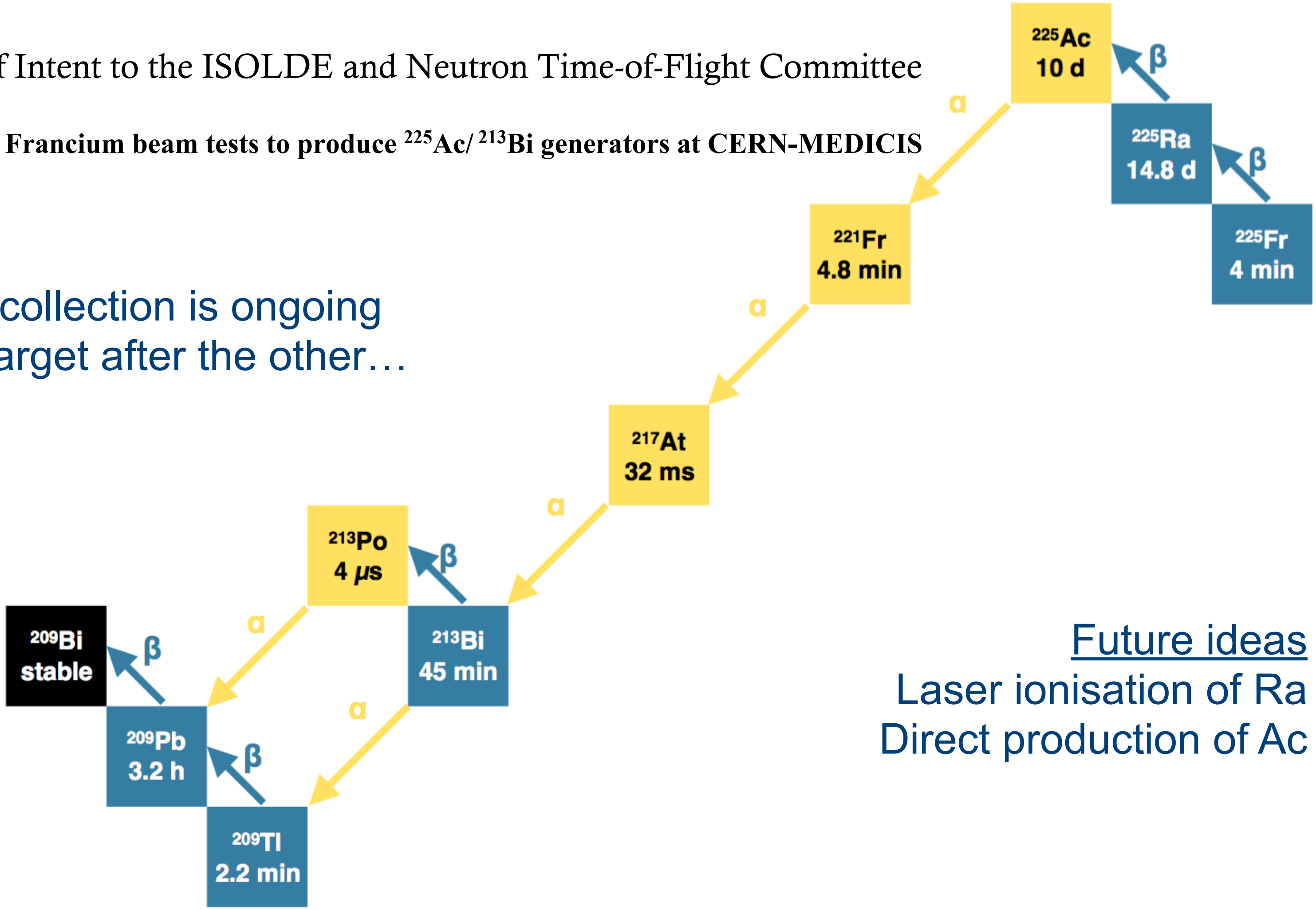




Alpha cancer therapy

Letter of Intent to the ISOLDE and Neutron Time-of-Flight Committee

Radium and Francium beam tests to produce ^{225}Ac/ ^{213}Bi generators at CERN-MEDICIS



I164

Data collection is ongoing
one target after the other…

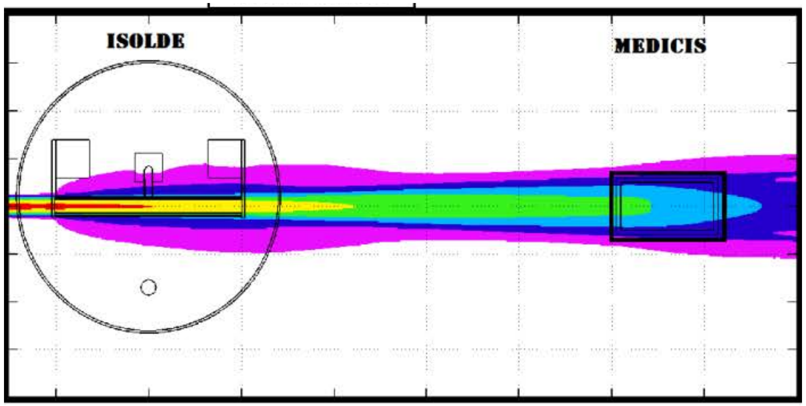
Future ideas

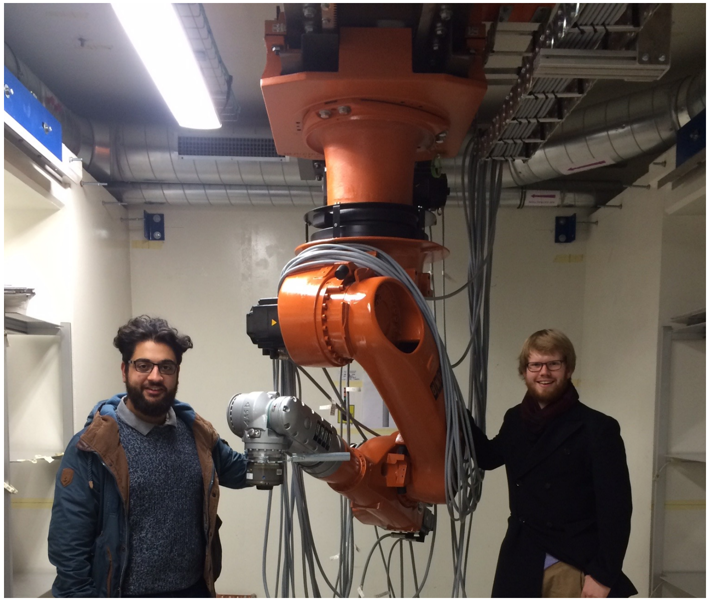
Laser ionisation of Ra
Direct production of Ac

CERN MEDICIS: MEDical Isotopes Collected from ISolde

Free beam for "free" radioisotopes at CERN

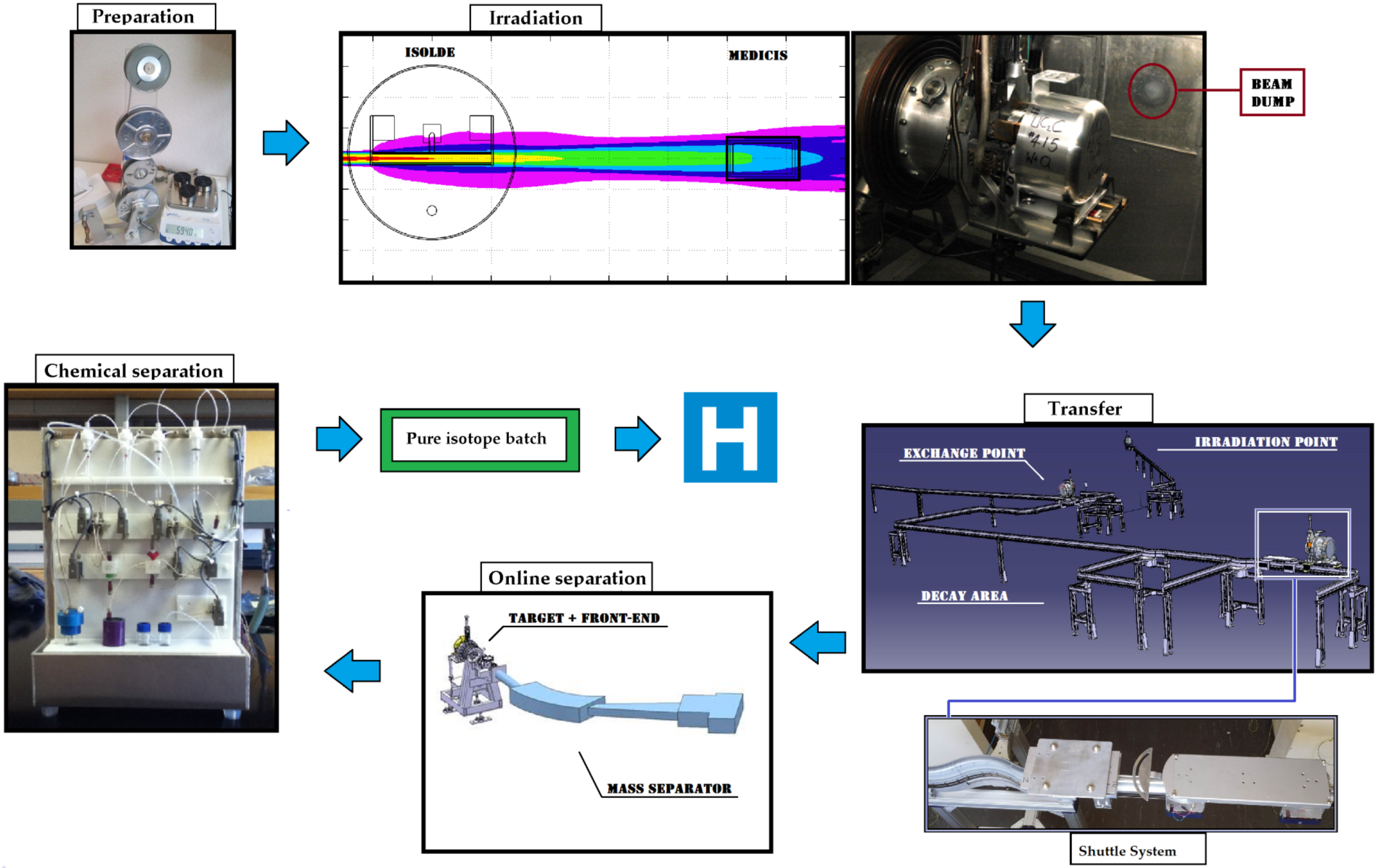
- 80% of the proton beam goes through the ISOLDE target unaffected
- That beam is then sent onto another target
- The target can be removed from the target area towards a Class A laboratory *(video)*
- An off-line separator is used to extract radioisotopes of interest





KU LEUVEN

CERN-MEDICIS from A to Z



Preparation

Irradiation

Transfer

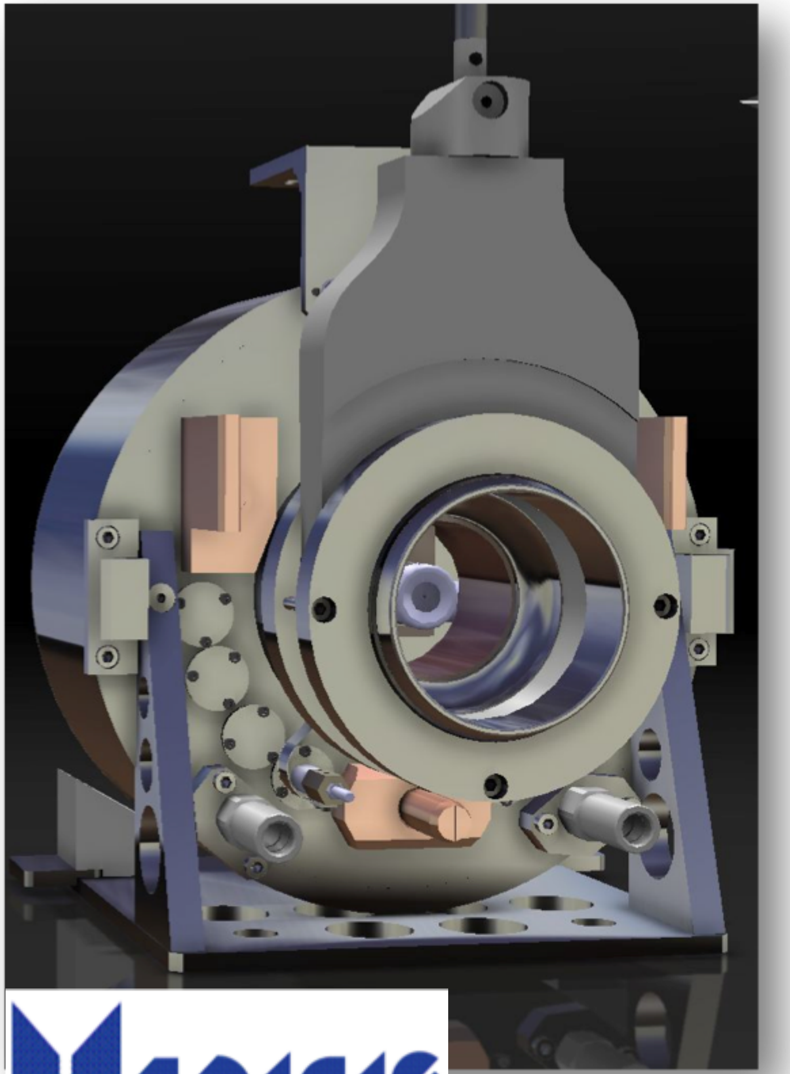
Shuttle System

Online separation

Chemical separation

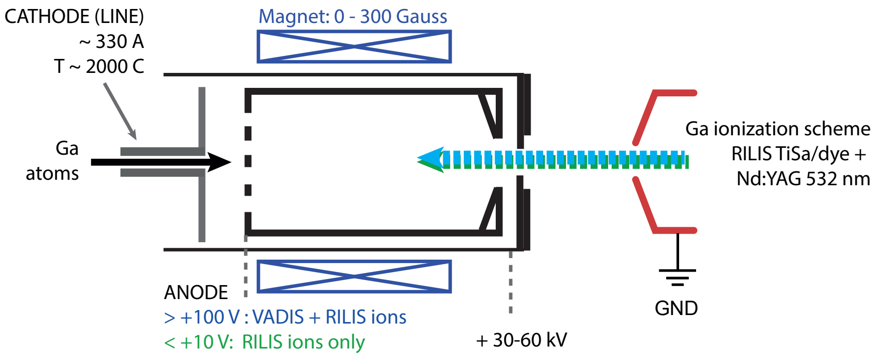
Pure isotope batch

CERN-MEDICIS: the ion source



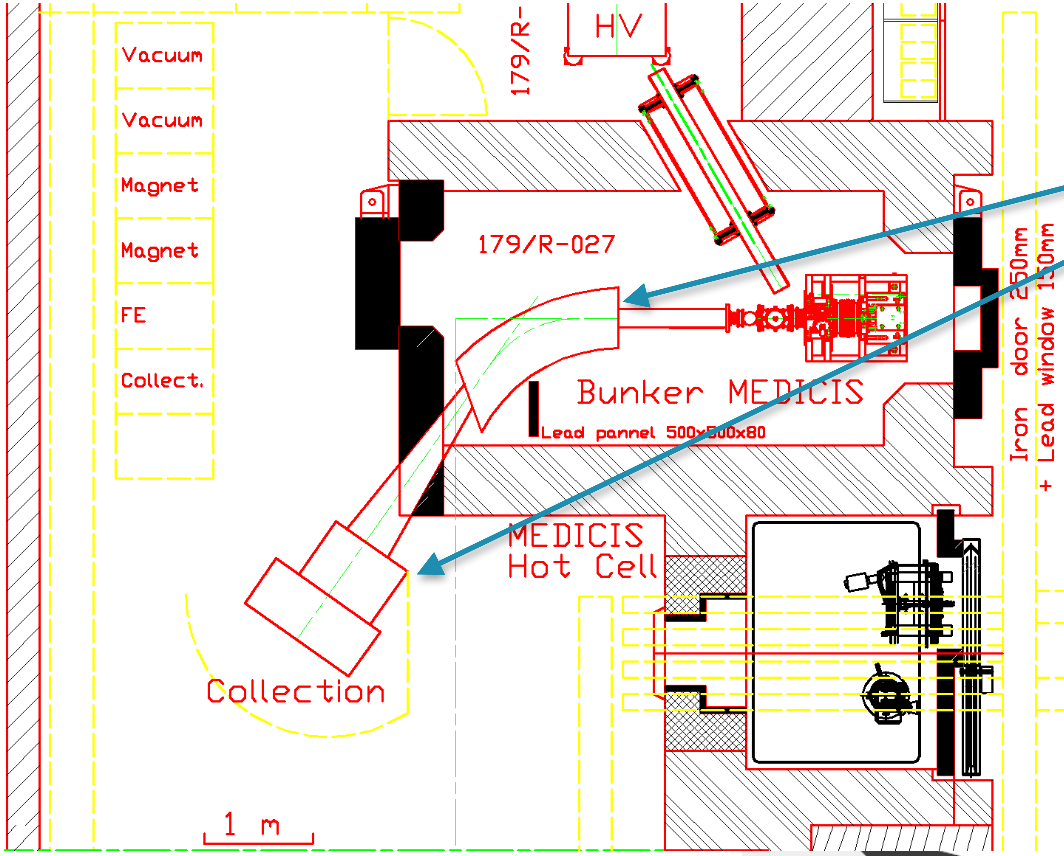
CERN-MEDICIS will use an ISOLDE-type target-ion-source module. For versatility, the choice of ion source is the VADIS, a plasma ion source that has demonstrated high efficiencies.

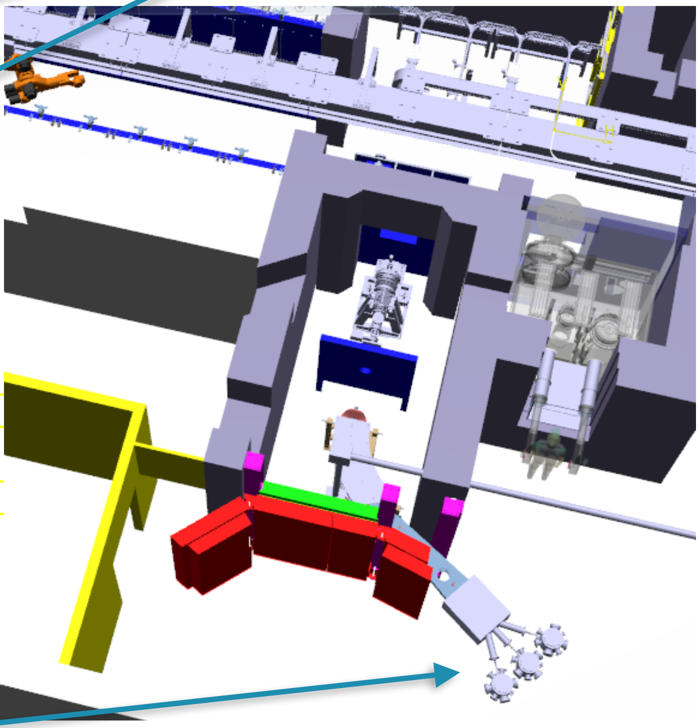
Recent developments by the ISOLDE Target Group, RILIS, and Windmill Collaboration have combined VADIS with laser ionisation. Further simulation and characterisation of this ion source are ongoing by a KU Leuven PhD student at CERN.



CERN-MEDICIS: the separator

Dipole magnet & switchyard from the LISOL separator, used for 40 years in Louvain-La-Neuve!





New collection chamber prototypes.

CERN-MEDICIS: Radiochemistry

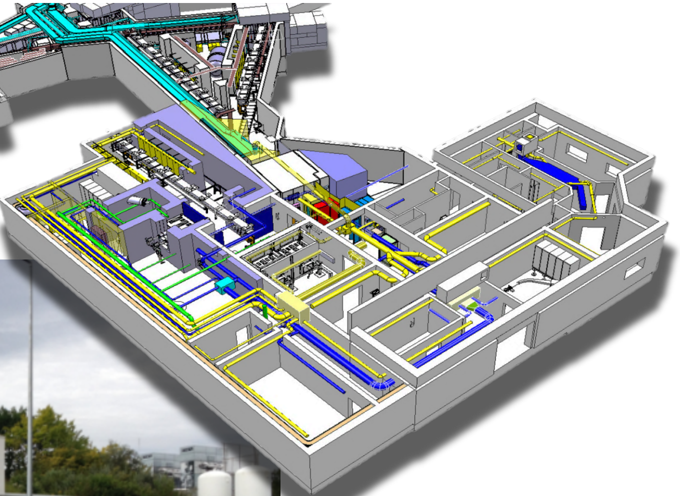
- The CERN MEDICIS collection hall will be equipped with shielded glove boxes.
- CERN is building up the knowledge around the use of these devices.
- Basic operations will be performed to provide medical teams with useable liquid samples.

- A large hot cell has also been installed to begin the dismantling of the accumulated ISOLDE targets.

MEDICIS timeline

Ground breaking
3 Sept 2013

Building delivered
15 Oct 2014

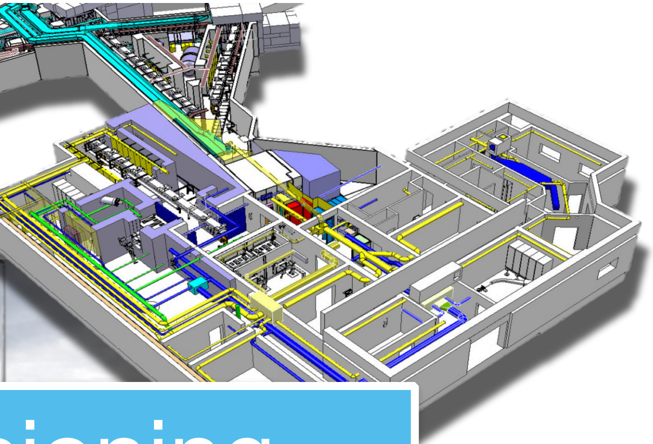


Separator delivered
28 June 2016

MEDICIS timeline

Ground bre
3 Sept 2

Building delivered
15 Oct 2014

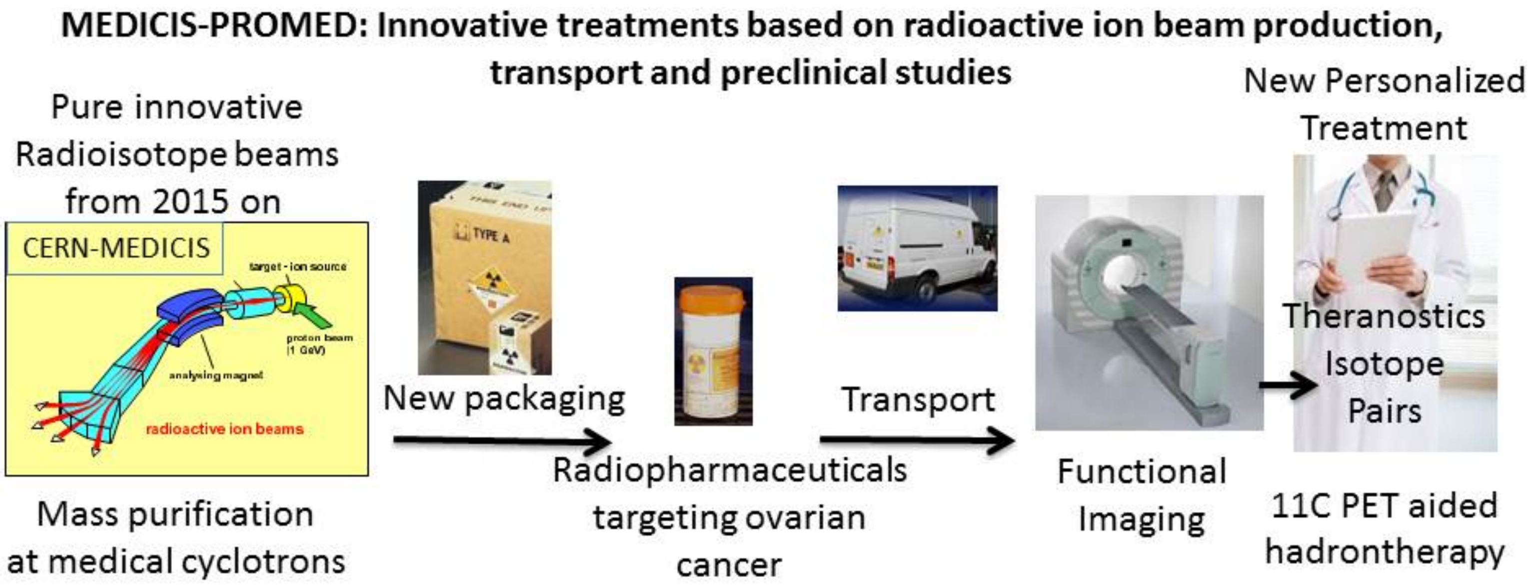


parator delivered
28 June 2016

Commissioning planned for 2017

MEDICIS-Promed

A Horizon2020 Marie Skłodowska-Curie Actions:
Innovative Training Network



MEDICIS-PROMED: Innovative treatments based on radioactive ion beam production, transport and preclinical studies

Pure innovative Radioisotope beams from 2015 on

CERN-MEDICIS

Mass purification at medical cyclotrons

New packaging

Radiopharmaceuticals targeting ovarian cancer

Transport

Functional Imaging

New Personalized Treatment

Theranostics Isotope Pairs

11C PET aided hadrontherapy

— CERN — The University of Manchester — University of Mainz —
— AAA — C2TN — CNAO — Lemer Pax — KU Leuven —
— CHUV — HUG — EPFL — Medaustron —
— Oxford University Consulting — ARRONAX — ILL —

CERN MEDICIS catalog

Isotope production at CERN MEDICIS.

Medical Application	Isotope half-life	Parent isotope beam	Target - Ion source	ISOLDE†		RIB Ɛext** (%)	CERN-MEDICIS†		CERN-MEDICIS 2GeV 6μA			Comments
				In-target								
				Production rate (pps)	Activity EOB (Bq)		In-target Activity EOB (Bq)	Extracted Activity# EOB (Bq)	Possible gain Ɛext (%)	In-target Activity EOB/	Extracted Activity# EOB (Bq)	
α,β- therapy/ SPECT/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
α,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*
Auger 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
β-/Auger 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
β- 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
β 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
α 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
^{140}Pr-PET/ Auger 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
β- 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
β- 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
β 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, dosimetry, therapy	^{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
PET	^{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
β 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◊	-	-	- 15	-	1.4E9	-	-	4.2E9	Only mass separation

Beyond novel medical radioisotopes

CERN MEDICIS Operation

- The production of radioisotopes at CERN MEDICIS is foreseen to last 30 weeks per year.
- Medical radioisotopes have priority.
- A board will decide of the science cases and a coordinator will make up the schedule.
- Activities will be reported via the INTC to the CERN Research Board.
- High-dose samples will be collected (much higher than at GLM, up to 10 GBq!) => Access will have to be limited to highly trained specialists.

Alternative use of the separator

- The off-line separator may also be used to separate other samples rather than just targets irradiated at ISOLDE, e.g. discussions are open with nToF for the purification of ^{204}Tl targets (contains >95% ^{203}Tl).
- During LS2, targets irradiated at other facilities could be brought to CERN MEDICIS to keep the activity going (e.g. from ARRONAX in Nantes, France, or iThemba LABS in South Africa).
- Any other element that may be produced at ISOLDE and which half-life is not too short is potentially accessible.

Mössbauer wish list…

^{57}Co

- 272 day half-life
- Online yields of 3×10^6 (ZrO_2) to 10^7 (Y_2O_3) ions per uC from a plasma source (MK5 or VADIS)
- Laser excitation schemes exist

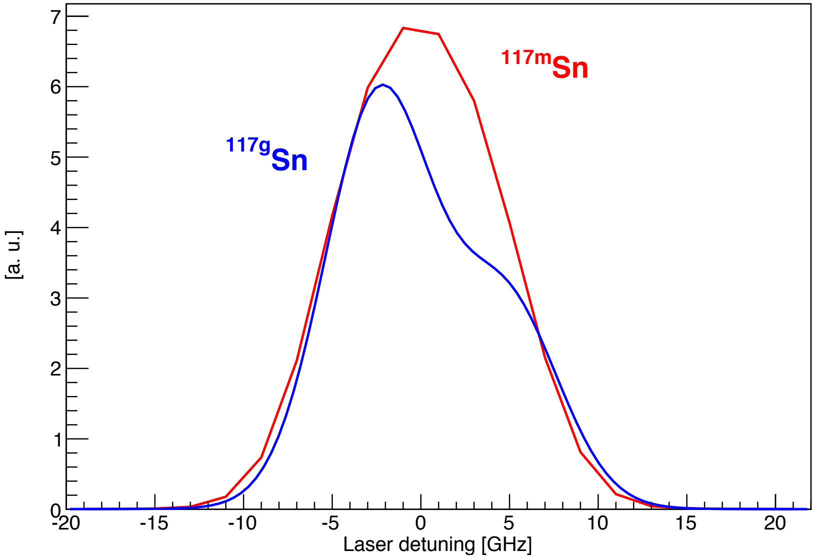
- Possible contamination: ^{57}Fe (stable) produced via plasma ionisation

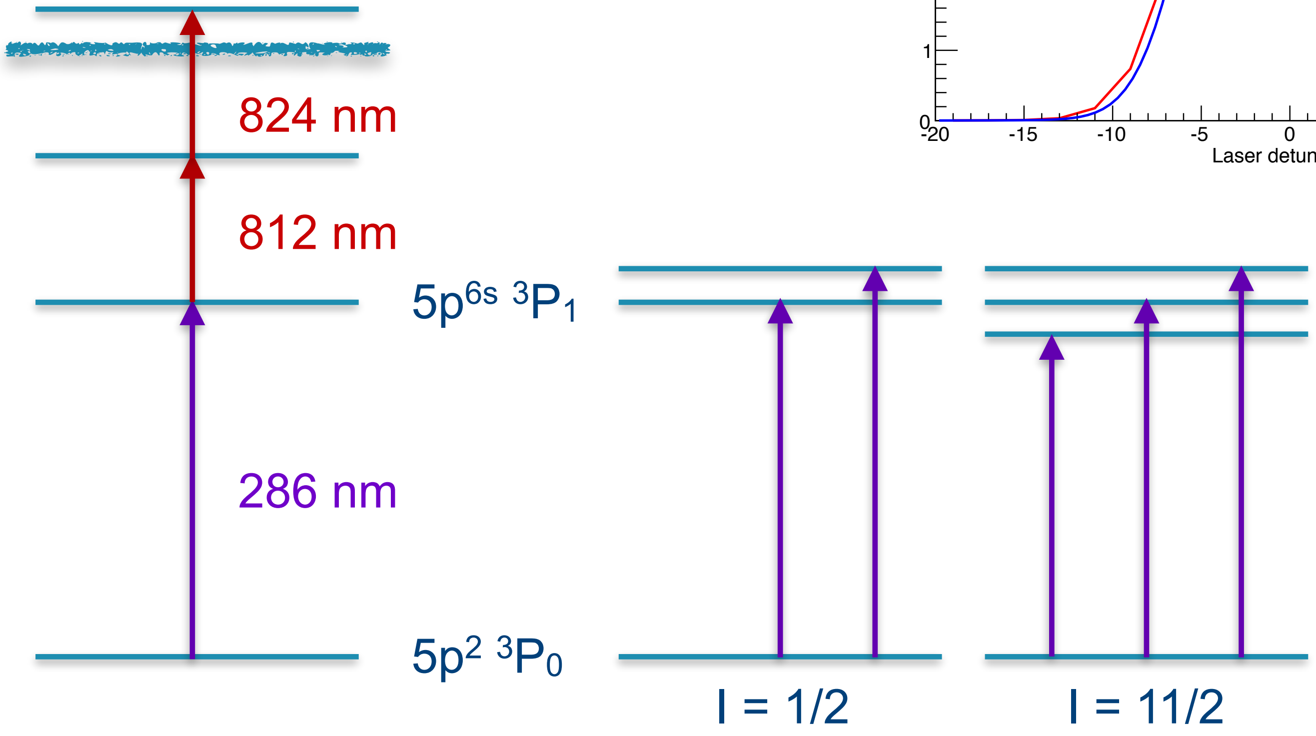
^{119m}Sn

- 293 day half-life
- Online yields unknown but would expect ~10^7 ions per uC
- Possible targets include LaC, Ta and UCx
- Laser excitation schemes exist

- Possible contamination: ^{119g}Sn (stable)
- ➡ RILIS in narrow-band mode for isomer separation?

^{119g}Sn vs ^{119m}Sn





824 nm

812 nm

5p^{6s} ^{3}P$_{1}$

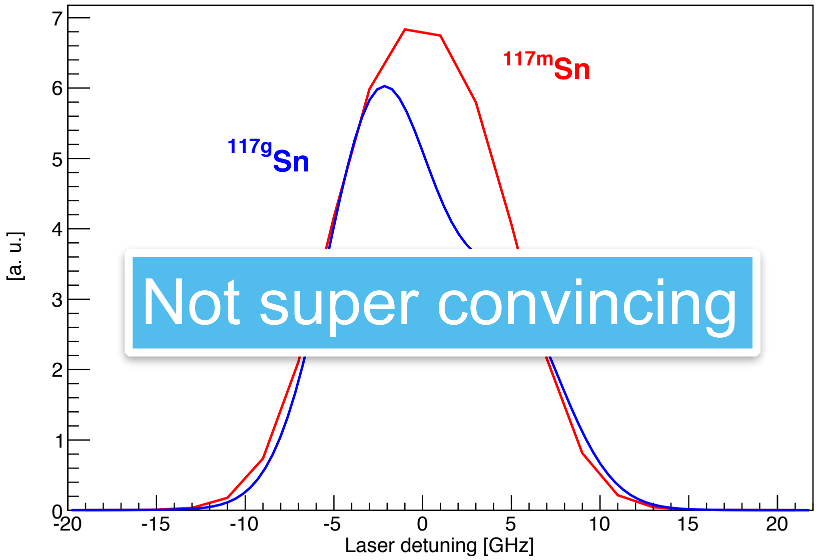
286 nm

5p^{2} ^{3}P$_{0}$

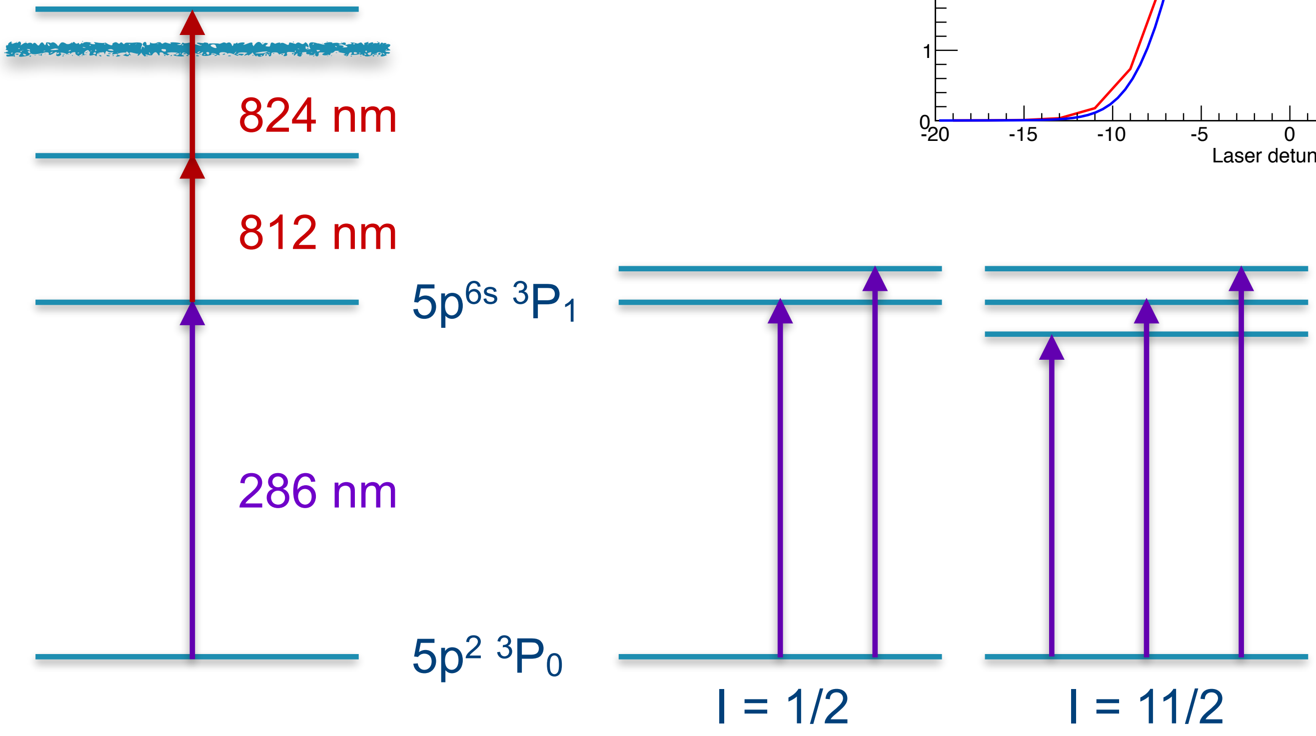
I = 1/2

I = 11/2

^{119g}Sn vs ^{119m}Sn



Not super convincing



824 nm

812 nm

286 nm

$5p^{6s}\ ^3P_1$

$5p^2\ ^3P_0$

I = 1/2

I = 11/2

The development of novel medical radioisotopes for **theranostics** & **alpha therapy** requires to provide a catalog of radioisotopes for research.

CERN MEDICIS is a new offline separator for parasitic operation next to ISOLDE, which will provide isotopes for medical research 30 weeks per year.

Alternative use of this separator can be foreseen, of potential interest to other communities, though the specific requirements for each sample must be considered.

Operation & safety are also concerns that must be evaluated carefully.