Use of alpha particle beams in medical radionuclide production

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2nd International Workshop on Proton-Boron Fusion (IWPBF)- Catania, Italy - Sept 05-08, 2022

Outline

- Quick recall about the use of α beams in industry
- Use of α beams in radionuclides' (RNs) production in Nuclear Medicine (NM)
- Some key facts about RNs for NM
- The RNs world market for NM
- Established/emerging RNs production pathways for NM
- The LARAMED project INFN LNL
- Some examples of RNs produced by alternative (α, X) nuclear reaction routes
- Main requirement for a laser-driven (p-11B) ->3α source for RNs production for NM

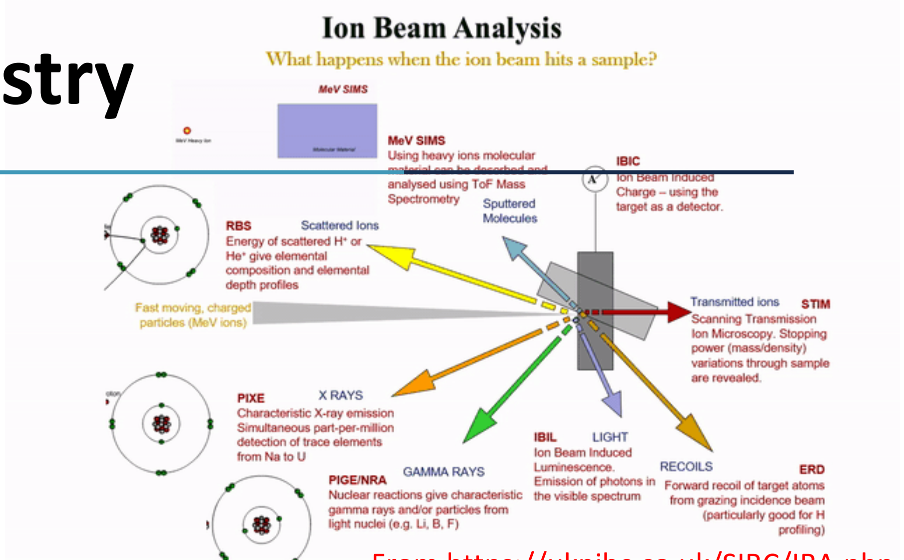
Brief recall about the use of α beams in industry

The use of α-particles beams from a few MeV up to 25/30 MeV, has found valuable applications in the last decades in many fields, ranging from **material characterization analyses** up to some **manufacturing process** in the industrial sector:

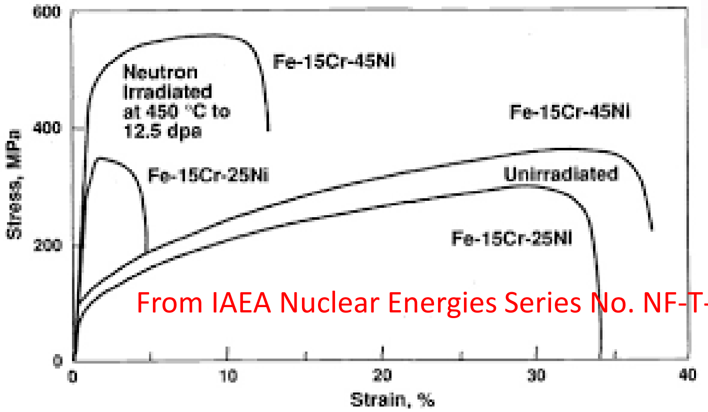
1. **Ion Beam Analyses (IBA) → RBS, ERDA, PIXE PIGE…..**
2. **New materials (i.e., composite ones) development →**, resistance/hardness performance modifications in micro-nano structured materials that have application in different sectors, like electronics, optics, aerospace, etc.
3. **Nuclear industry →** high damage level in the lattice of structural materials receiving high neutron fluence levels ($\geq 10^{18}$ cm^{-2}), located:
   a. close to core in fission fast nuclear reactors;
   b. in the blanket region of future (e.g. ITER/DEMO) fusion power reactors,

caused by (n,xα) reaction routes→, large productions of helium gas. These processes are still very little known.

Accelerators (or alternative sources) able to provide 20 MeV or larger α-particle beams with nA up to mA intensities may allow to conduct such studies.

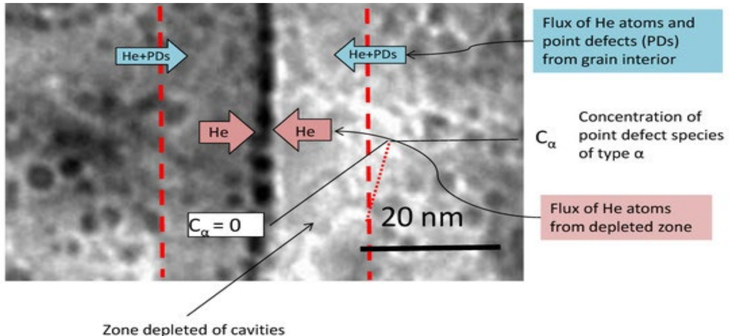


From https://uknibc.co.uk/SIBC/IBA.php



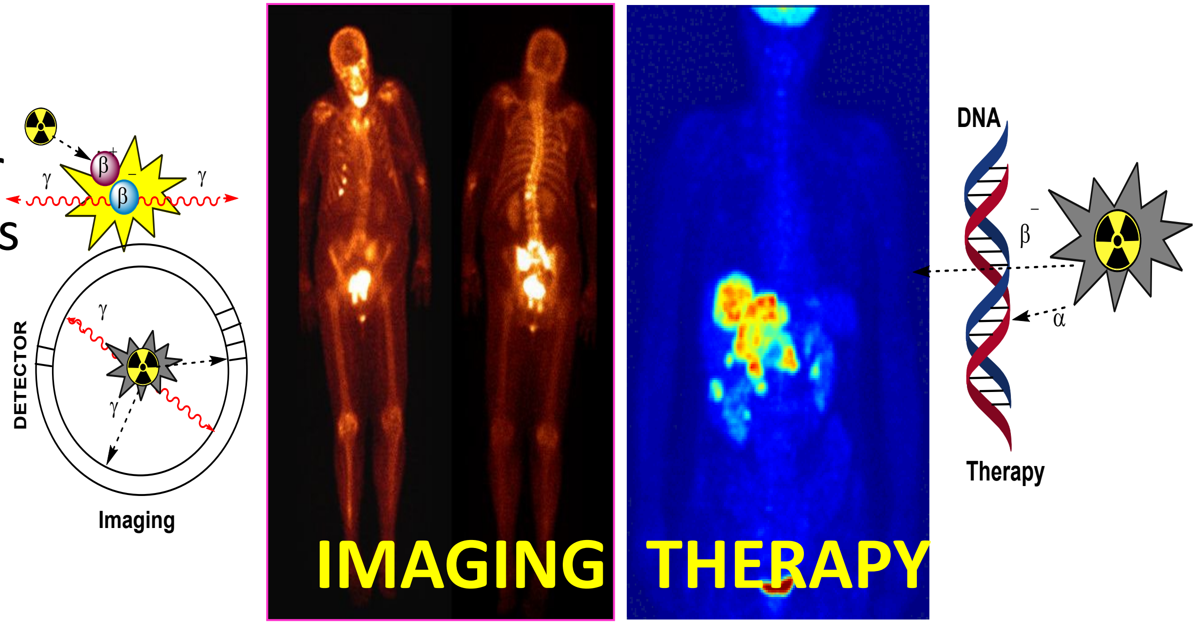
From IAEA Nuclear Energies Series No. NF-T-2.2

From Malcolm Griffiths, *Materials* **2021**, *14*(10), 2622; https://doi.org/10.3390/ma14102622



Other potential use of α-beams: emerging radionuclides (RNs) production for Nuclear Medicine (NM) applications

- The new frontier of NM is the "**theranostic approach**", i.e. RNs combining properties specific for imaging and those for radiotherapy (e.g. local tumors treatment) by using a **single radiopharmaceutical product**.



- The most important **theranostic RNs** known nowadays, i.e. having a nuclear decay pattern suitable for both applications are ^{47}Sc, ^{67}Cu, ^{64}Cu, ^{67}Ga...others...still to be found

THERAPY (+ DIAGNOSTIC) = THERANOSTIC

- The theranostic approach may be also obtained with **"theranostic pair"** i.e. Isotopic RNs, one specific for imaging, while the other one for therapy. The most known pairs belonging to this group are $^{43/44}$Sc/^{47}Sc, $^{61/64}$Cu/^{67}Cu, ^{68}Ga/^{67}Ga, $^{149/152}$Tb/$^{155/161}$Tb and others ...still to be found

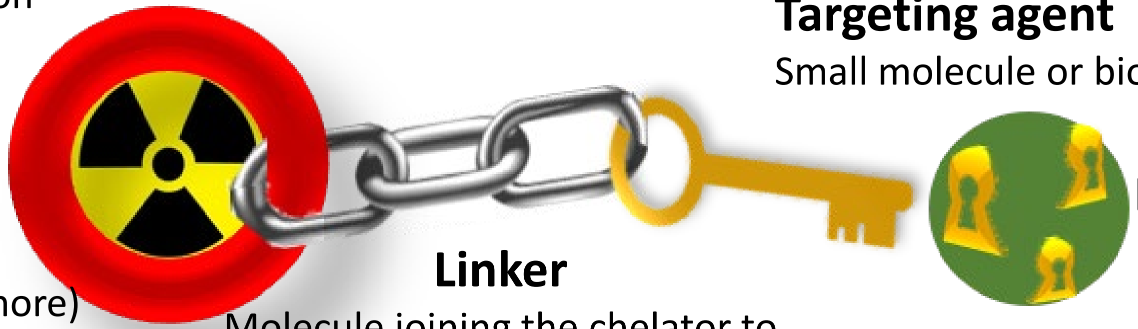
Radionuclides & Radiopharmaceuticals: the essential probes in NM

Radiopharmaceutical: how it’s made

Radioisotope
Provides the signal emission by decay radiation

γ-ray β^{+}	β^{-} α

Chelator
Molecule holding one (or more) radioisotopes in a stable way

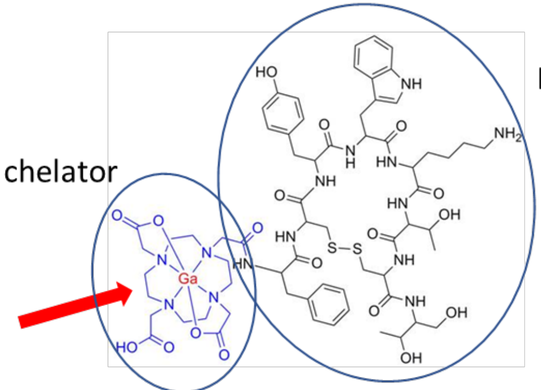


Linker
Molecule joining the chelator to targetting agent

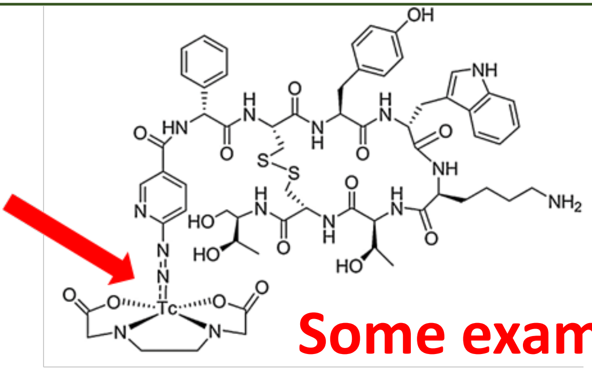
Targeting agent
Small molecule or biological agent (Ab, ecc..)

Biological target (e.g. tumors cells)

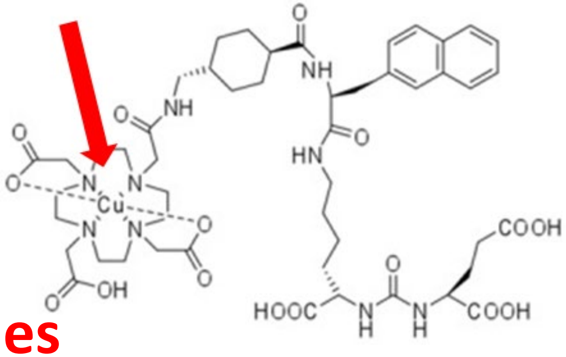
Better if overespressed by target cells

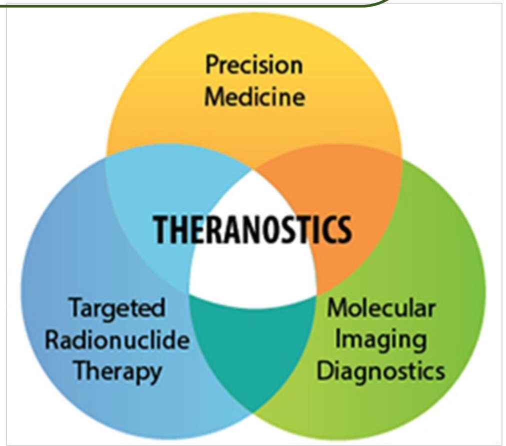


[^{68}Ga]Ga-DOTATOC


[^{99m}Tc]Tc-HYNIC-TOC

Some examples


[^{64}Cu]PSMA-617

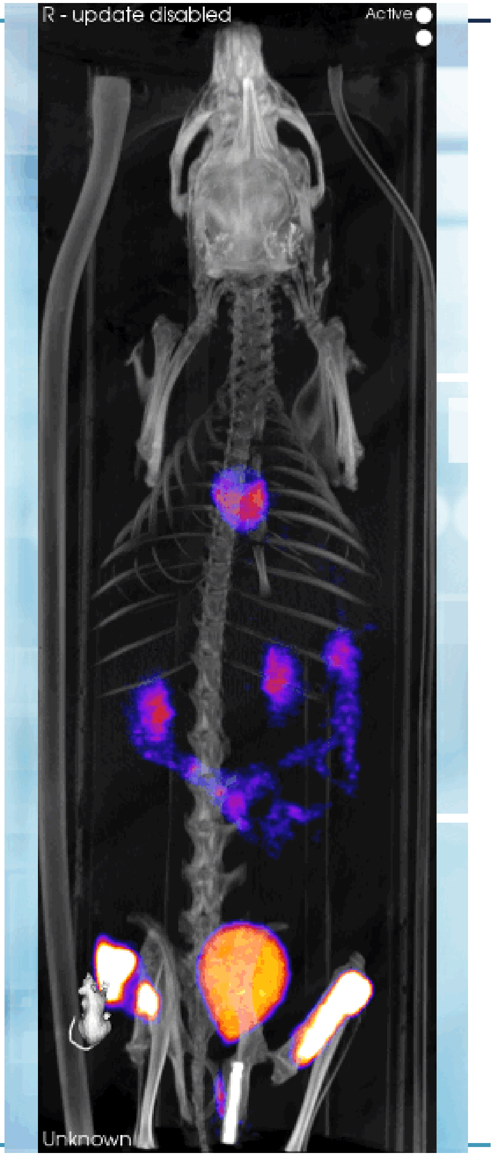


The new scanner technology of hybrid tomograph

SPECT/CT

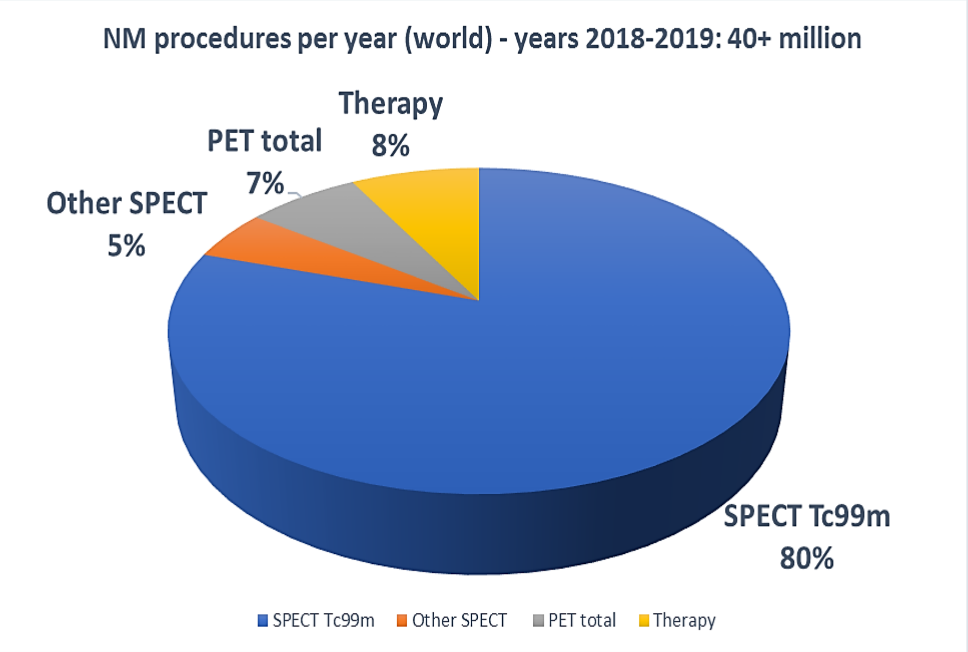
PET/CT

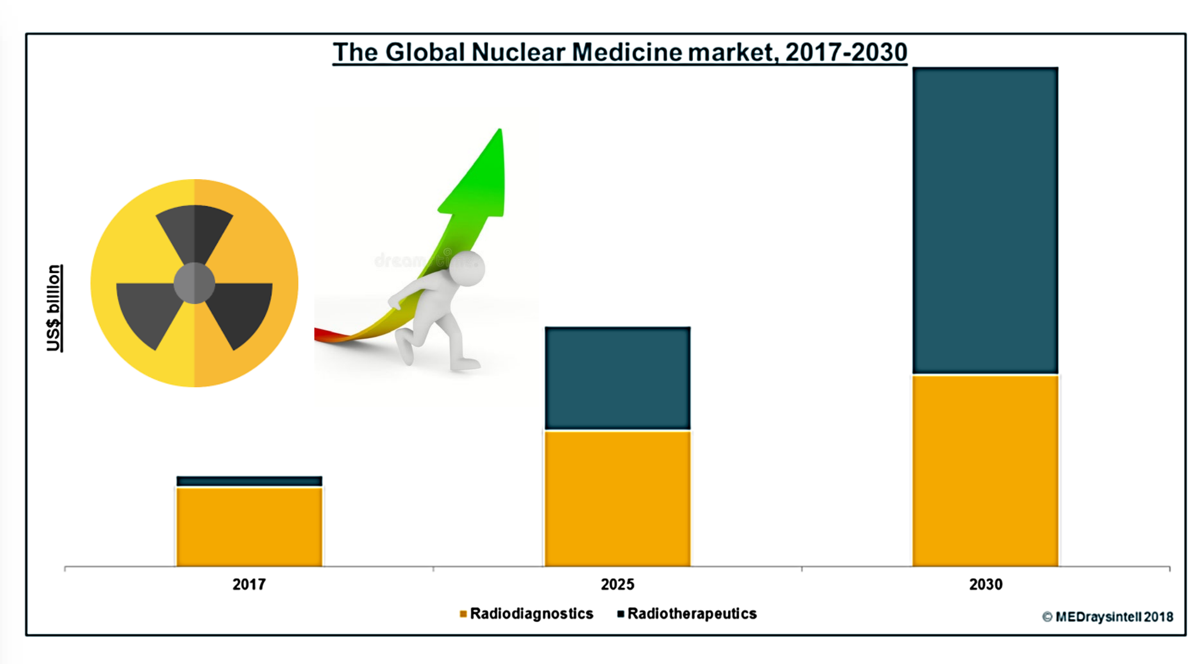
PET/MRI



NM procedures in the world: some reference data (pre COVID-19 yrs)

- In recent years (2018-2019) there have been about **40 MILLION clinical procedures in the world** making use of radionuclides **(about 13 every 10 seconds!!).**
  - The demand for RNs in NM is growing at a rate **~ 5% every year.**
  - The use of **radionuclides for imaging/diagnostic** grows by an average of **10% every year.**
  - In the USA more than **20 million procedures** are conducted per year while in the **EU there are about 10 million and in Australia, 560,000**.



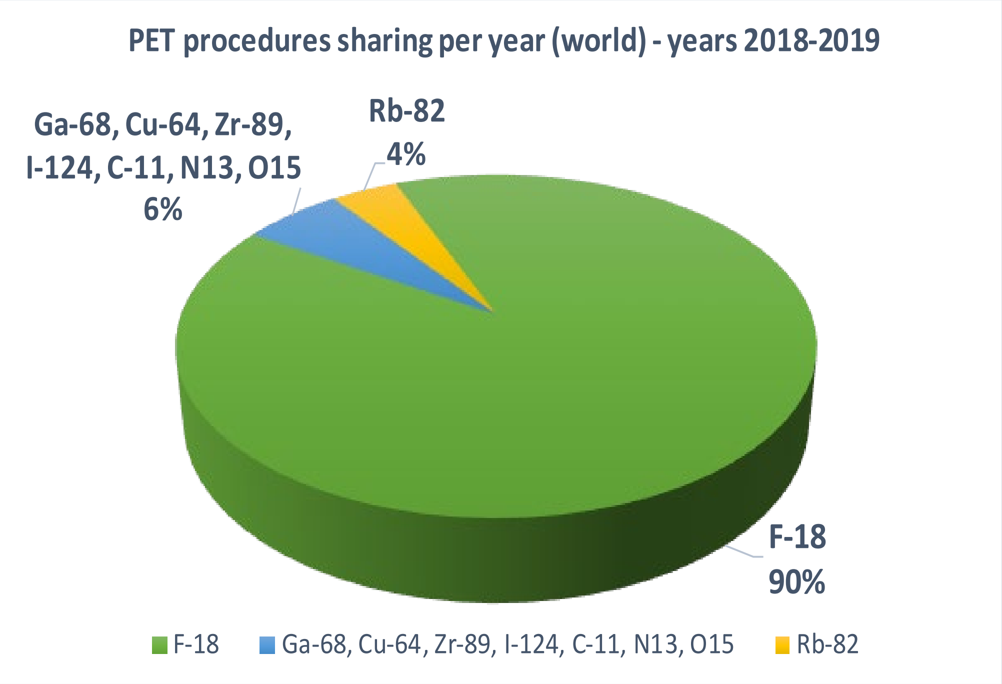


Source:
WORLD NUCLEAR ASSOCIATION (https://world-nuclear.org)
TECHNOPOLIS GROUP (https://www.technopolis-group.com/)
MEDraysintell (https://www.medraysintell.com/)

- The global NM market reached **~ 5 billion US$ in 2017**, with a growth trend (pre-Covid 19) of 5-7% (2016 data).
- Growth is estimated between **14 – 26 Billion US$ in 2030**

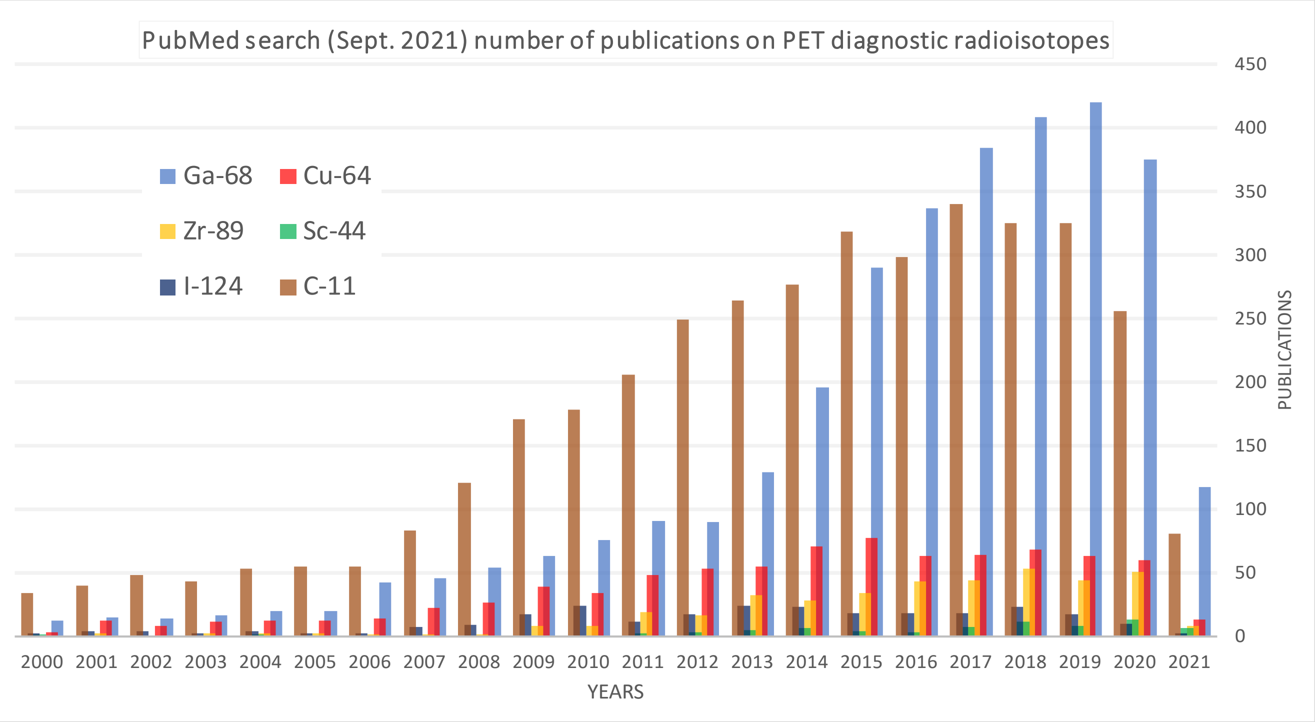
Trends in the search for new PET radionuclides: some reference data (pre COVID-19 yrs)

- The **expected growth rate (CAGR)** for the use of PET radionuclides in the coming years is of the order of 5% (2019 estimate)



Fonte:
WORLD NUCLEAR ASSOCIATION (https://world-nuclear.org)
TECHNOPOLIS GROUP (https://www.technopolis-group.com/)
MEDraysintell (https://www.medraysintell.com/)

- **Trends in publications** in the last **20 years (2000-2020)** regarding the clinical and research uses of PET radionuclides:



PubMED search engine (Sept. 2022)
Search criteria (e.g. Ga68): Search query: (68 Ga) OR (Ga 68) OR (68Ga) OR (Ga68) OR (68-Ga) OR (Ga-68) OR (68-Gallium) OR (Gallium-68)

Radionuclides used in Nuclear Medicine

Gamma-Emitting Radionuclides

Isotope	Half-life (hours)	Decay Mode*	production
Tc-99m	6.0	IT	generator
I-123	13.0	EC	cyclotron
Tl-201	73.5	EC	cyclotron
In-111	67.3	EC	cyclotron
Ga–67	78.3	EC	cyclotron

Alpha-Emitting Radionuclides

Radionuclide	Half-life	α Decay Energy (keV)	γ Decays Energy (keV)
Tb-149	4.12 min	4077	(β+) 352
At-2111	7.21 h	5867	79
Bi-212	60.6 min	8785	727
Bi-213	45.7 min	8378	440
Ra-223	11.4 d	5348	269
Ra-224	3.62 d	5094	241
Ac-225	10.0 d	5450	86
Th-226	30.9 min	6338	111
Th-227	18.7 d	5562	236
Fm-255	20.1 h	7022	16

Positron-Emitting Radionuclides

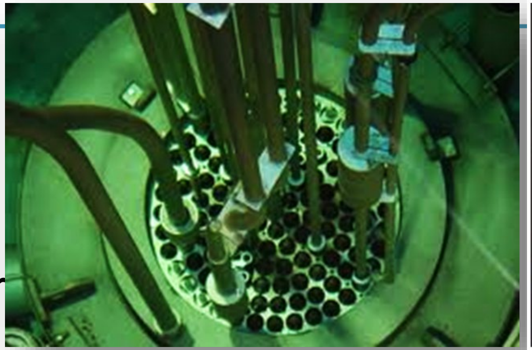
Isotope	Half-life	Max. Energy	range(mm)	production
C–11	20.4 mins	0.96 MeV	0.4 mm	cyclotron
N–13	9.96 mins	1.20 MeV	0.7 mm	cyclotron
O–15	123 secs	1.74 MeV	1.1 mm	cyclotron
F–18	110 mins	0.63 MeV	0.3 mm	cyclotron
Cu–62	9.74 mins	2.93 MeV	2.7 mm	generator
Cu-64	12.7 hours	0.65 MeV	0.3 mm	cyclotron
Ga–68	68.3 mins	1.83 MeV	1.2 mm	generator
Br-76	16.1 mins	1.90 MeV	1.2 mm	cyclotron
Rb–82	78 secs	3.15 MeV	2.8 mm	generator
I–124	4.18 days	1.50 MeV	0.9 mm	cyclotron

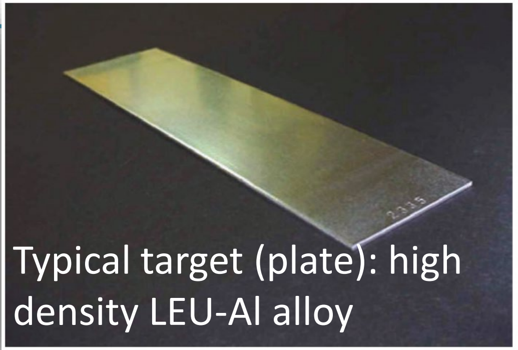
β-emitting Radionuclides

Radionuclide	Half-life	Mode of decay	$E_{\beta max}$ (keV)
^{90}Y	64.00 h	β^-	2280.1
^{131}I	8.02 d	β^-, γ	970.8
^{153}Sm	46.28 h	β^-, γ	808.4
^{89}Sr	50.53 d	β^-	1496.6
^{177}Lu	6.73 d	β^-, γ	498.3
^{188}Re	16.98 h	β^-, γ	2120.4
^{186}Re	3.72 d	β^-, γ	1069.5
^{32}P	14.26 d	β^-	1709.0

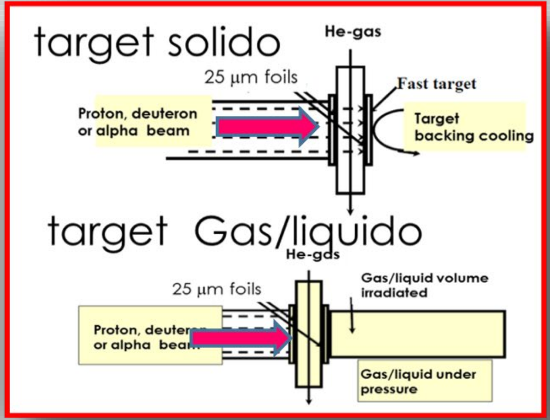
Some key points about established/emerging RNs production for NM

- Most of RNs nowadays used in NM are massively produced by **using nuclear reactors** (e.g., Mo99/Tc99m generators, the most used radionuclide worldwide).



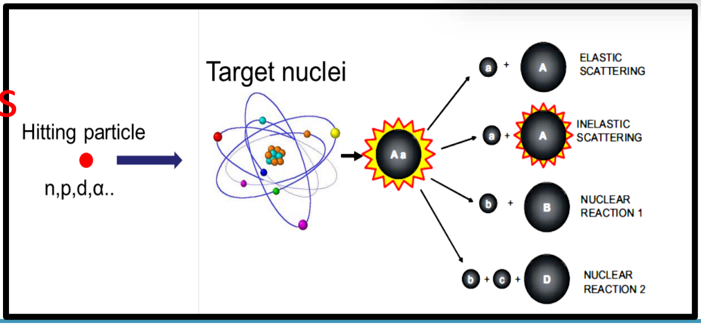


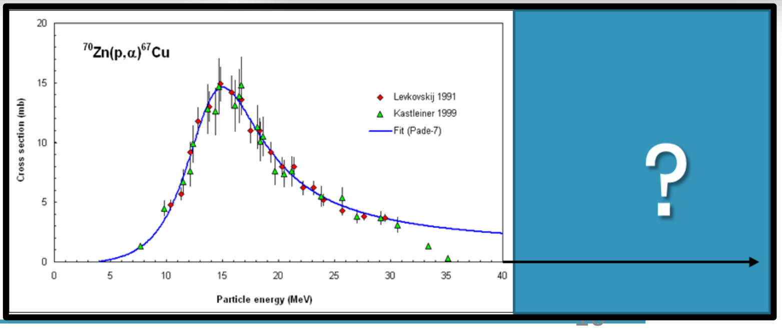
- **Particles accelerators (p,d,alpha …..), e.g.cyclotrons/linacs (or e-linacs producing a** γ-source) are becoming the alternative supplying route of choice. (in some cases, the only way). Not only for already established RNs, but also for the **new emerging RNs.**



- To select **the optimal RNs' production pathway,** it is **mandatory to probe all the possible nuclear reaction routes (xs measurements)** and determine the full map of isotopic contaminants.

- For most of them optimal production routes still needs to be cleared/investigated.





Production of established/ emerging RNs in NM (some examples)

Most accelerator-based radionuclides are nowadays, produced by public/private facilities by using **proton beams**:

- **large network of low-energy Small Medical Cyclotrons (SMC)** (Ep<20 MeV) based upon the well-established **H- ion source technology** (100% efficiency extraction by using stripper foils)
  → e.g. **ACSI TR19/300** Sacro Cuore Don Calabria Hospital (Negrar, VR) or **IBA 18/9** (e.g. LENA, Pavia,Italy);

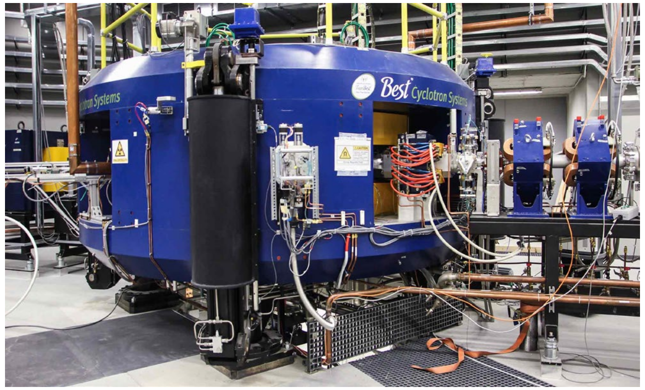
- some **mid-energy p,d,(α)** cyclotrons (i.e. Ep 20-35 MeV)
  → e.g **IBA Cyclone -30**, Kolkata Research Center, India;

- a few **high-energy p,d,(α)** cyclotrons (i.e. Ep>35 MeV)
  → e.g. ARRONAX (France), ZEVACOR (Us), LARAMED (Italy)

ACSI TR 19/300 Cyclotron

Protons: 14-19 MeV, >300 μA (up to ~6 kW)
Possible dual particle accelerations
Radiopharmacy and cyclotron unit Sacro Cuore Don Calabria Hospital, Negrar (VR) , Italy

The Cyclone-30 (15-30 MeV, 350μA max) isotope-producing cyclotron, Kolkata-based VECC India



The BEST BCSI 70p: dual exit port cyclotron,
- H^- 35-70 MeV, 750μA max
- D^- future installation
- $^4He^{2+}$ future installation

SPES/LARAMED facility, Legnaro (Padua),Italy

The IBA Cyclone-70: dual exit port
- H^- 30-70 MeV, 750μA max
- D^- 15-35 MeV 50μA max
- $^4He^{2+}$ 70 MeV 35μA max

isotope-producing cyclotron, ARRONAX, Nantes, France

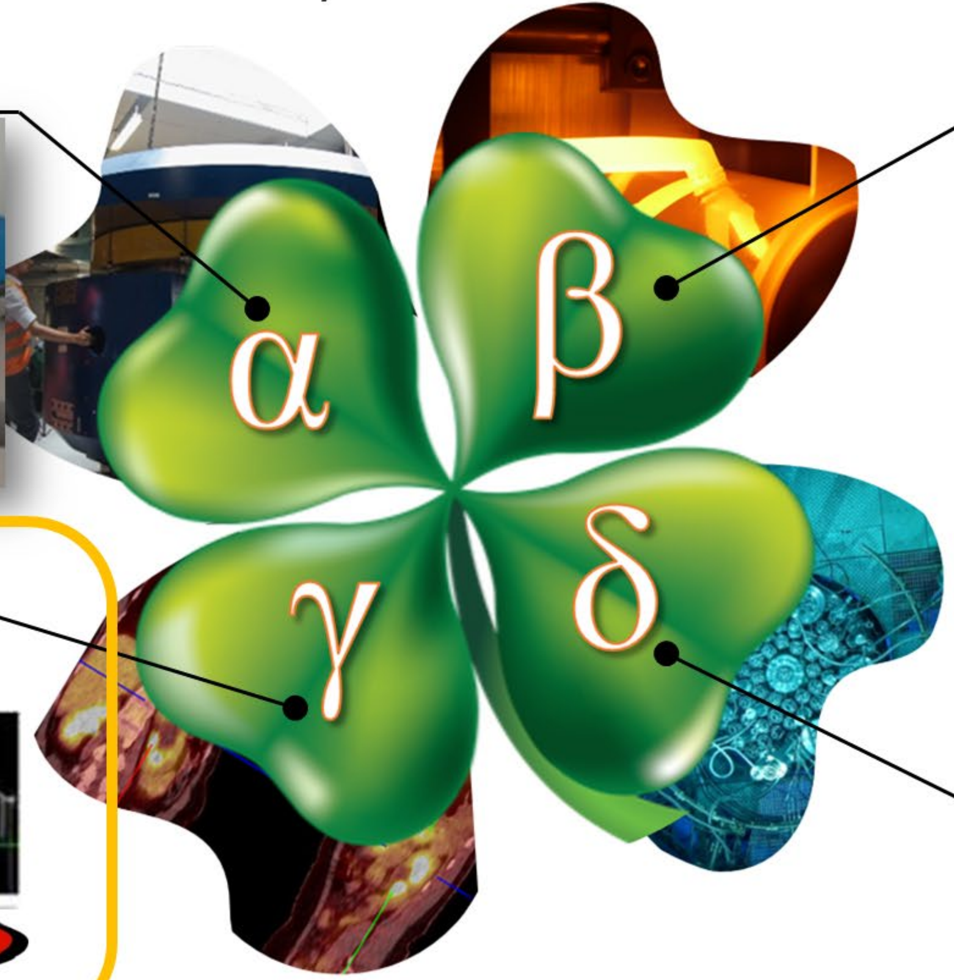
The new research infrastructure SPES @ LNL: Selective Production of Exotic (nuclear) Species

accelerator facility for research activity in different fields...

SPES exotic beams for science

SPES-α

Cyclotron installation and commissioning (and related infrastructure)

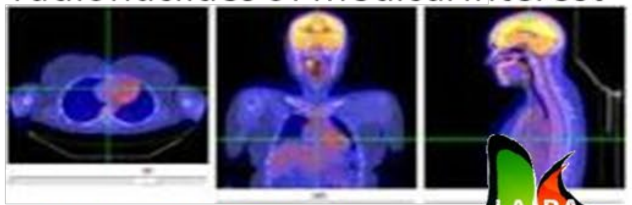


SPES-β

The ISOL facility and the acceleration of neutron-rich unstable nuclei.

SPES-γ

Study and production of novel radionuclides of medical interest

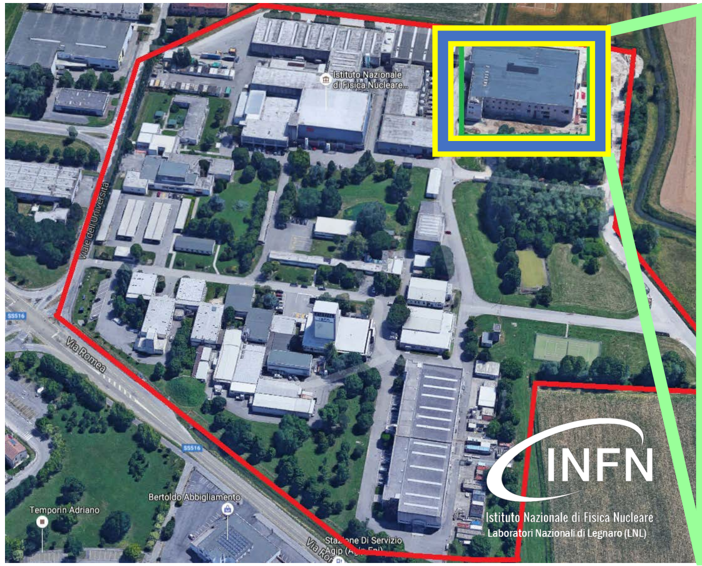


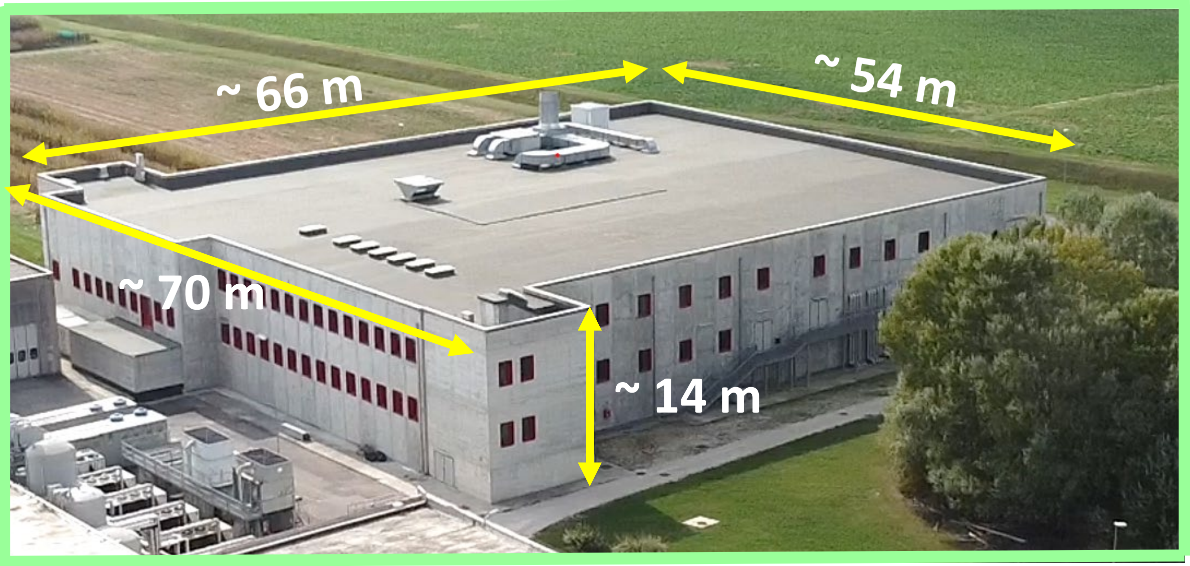
ISOLPHARM SPES exotic beams for medicine & LARAMED

SPES-δ

Neutron sources for material study, nuclear technologies and medicine

The SPES/ LARAMED infrastructure status (work in progress….)





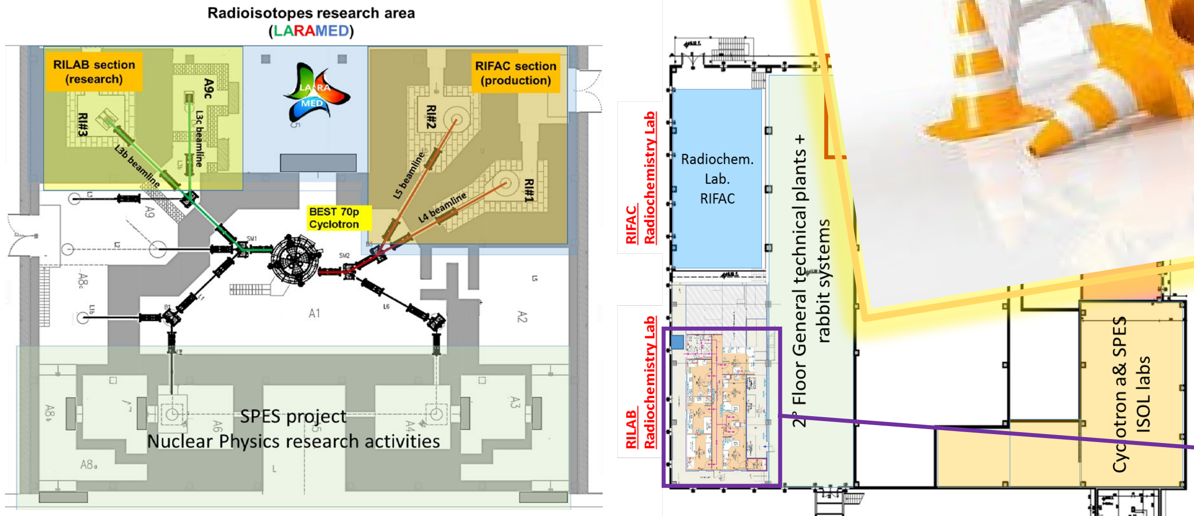
The LARAMED project at INFN-LNL

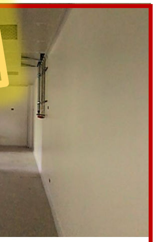
The BCSI 70p, p-cyclotron **(35-70 MeV, 750µA)**
dual exit port cyclotron

Research and technological development for innovative radionuclide

DIRECT technology

LAboratory of
Radionuclides for
MEDicine





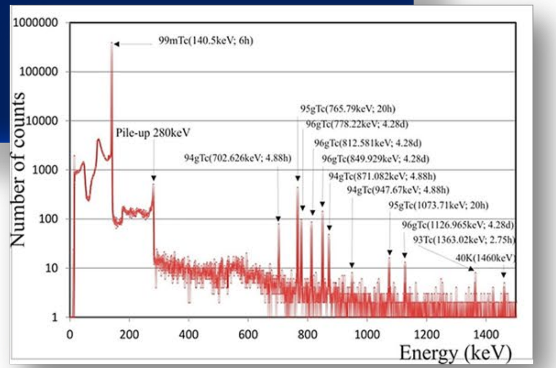
RILAB chemistry / targetry labs

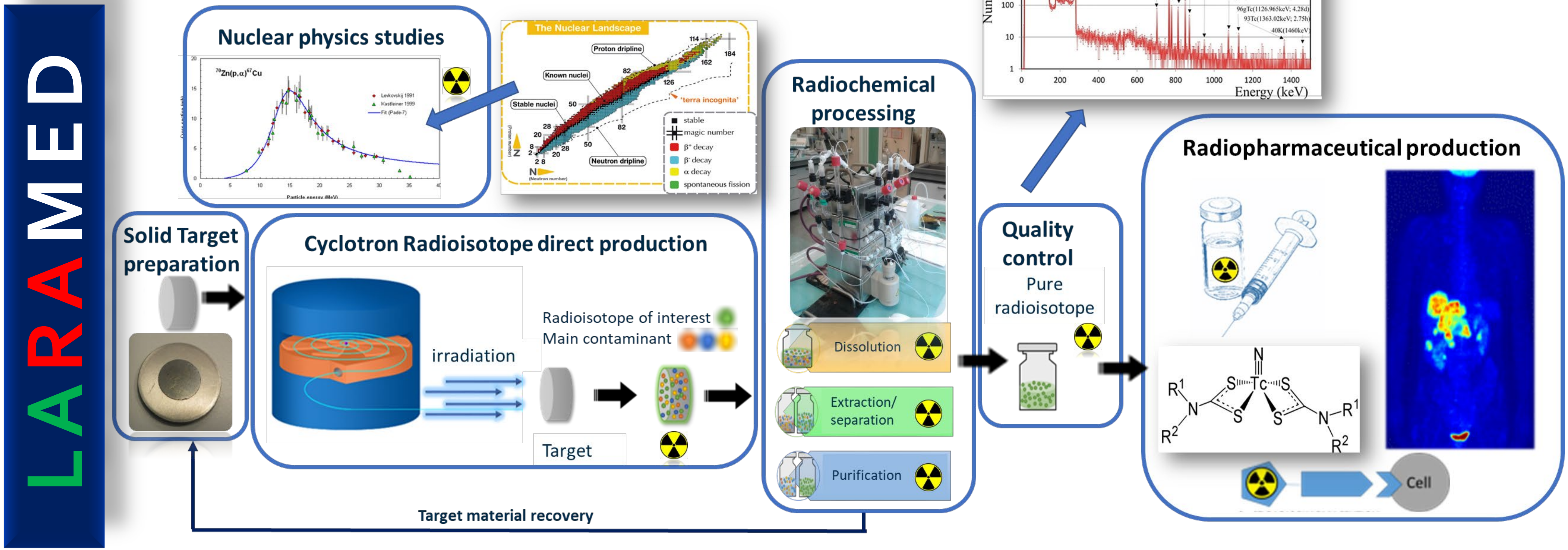
RILAB radiochemistry lab

Esposito et al., LARAMED: A Laboratory for Radioisotopes of medical interest, Molecules 2019

LARAMED : the radionuclides direct production route…

Capable of producing several radionuclides (different isotopes and chemical species) **in**
- **large radioactive amounts**
- **high/good quality (i.e. high Radionuclidic purity & Specific activities)**





Current radionuclides under the spotlight of LARAMED project

Tc-99m	Sc-47	Mn-52/51	Tb-149/52/55/61	Cu-67/64/61
APOTEMA / TECHNOSP	PASTA	METRCIS	REMIX	COME/ CUPRUM-TTD

J. Esposito et al, Molecules2019, 24(1), 20

molecules MDPI

Letter

LARAMED: A Laboratory for Radioisotopes of Medical Interest

Juan Esposito [1], Diego Bettoni [1,2], Alessandra Boschi [3], Michele Calderolla [1], Sara Cisternino [1], Giovanni Fiorentini [2], Giorgio Keppel [1], Petra Martini [1,3,*], Mario Maggiore [1], Liliana Mou [1], Micòl Pasquali [1], Lorenzo Pranovi [1], Gaia Pupillo [1], Carlos Rossi Alvarez [1], Lucia Sarchiapone [1], Gabriele Sciacca [1], Hanna Skliarova [1], Paolo Favaron [1], Augusto Lombardi [1], Piergiorgio Antonini [1] and Adriano Duatti [1,4]

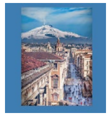
Best Theratronics

The brand new B70 cyclotron: Installed in May 2015, commissioning completed on Sept.2017

Dual simultaneously beam extraction cyclotron (E_P = 35-70 MeV):

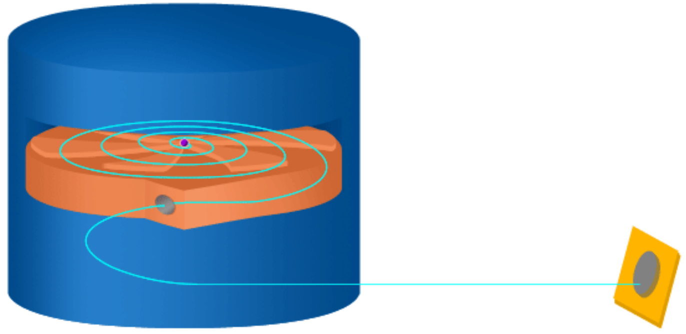
1° - nuclear physics research on RIBs **(SPES project)** : **E=40 MeV , I=200 μA** (and future upgrades)

2° - applied physics **(LARAMED project**, neutron source) : **E=35-70 MeV , I=300 μA** (upgrade 500μA)

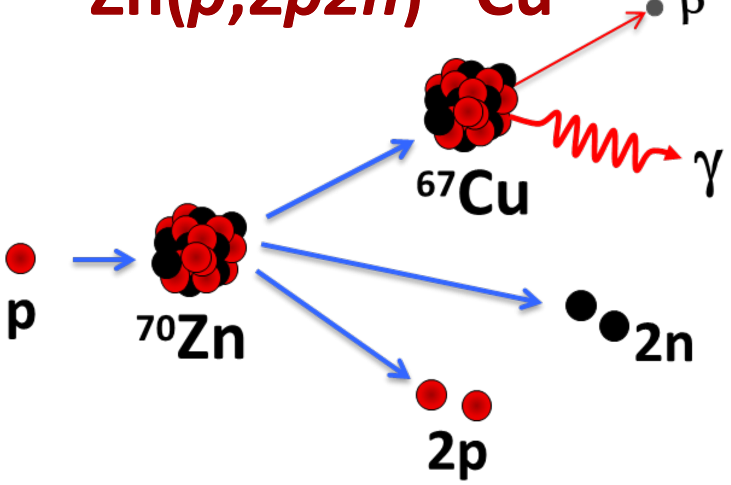


Accelerated α-beams: a new route for emerging RNs production for NM

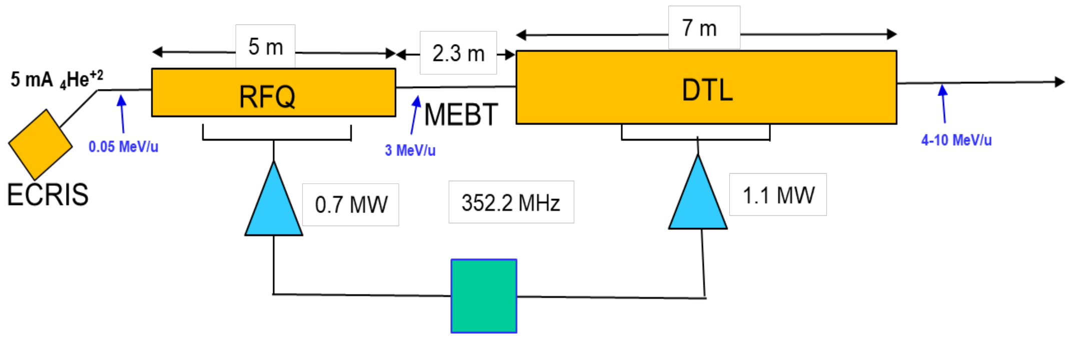
Proton/deuteron cyclotron



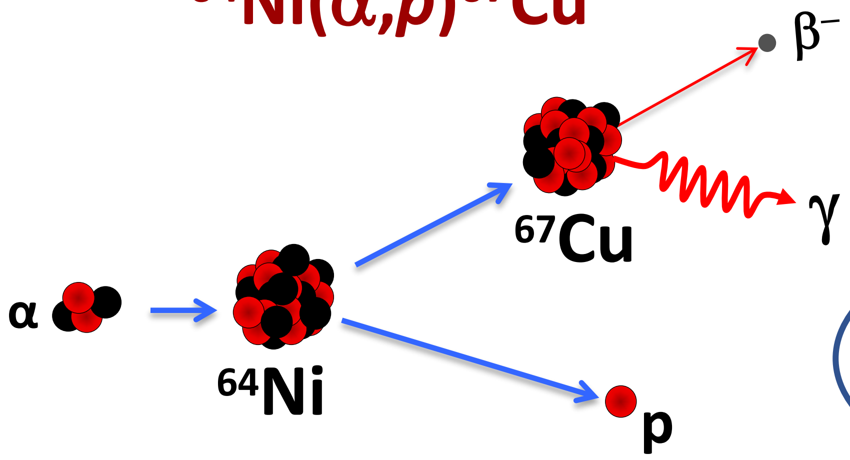
$^{70}Zn(p,2p2n)^{67}Cu$



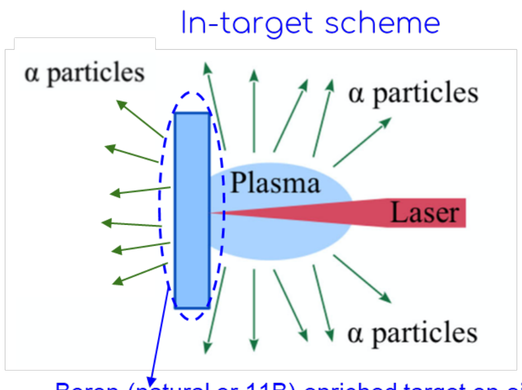
Alpha-DTL (up to 10 MeV/u at least)



$^{64}Ni(\alpha,p)^{67}Cu$



p-11B ->3α fusion sources

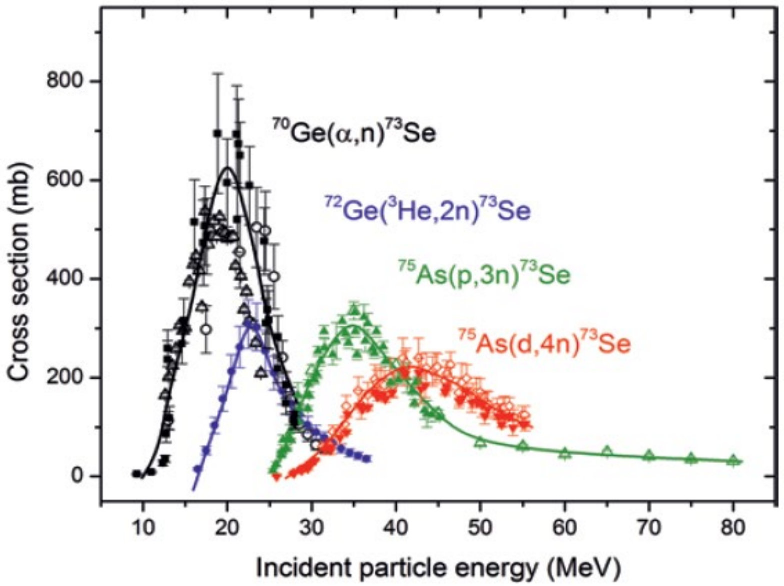


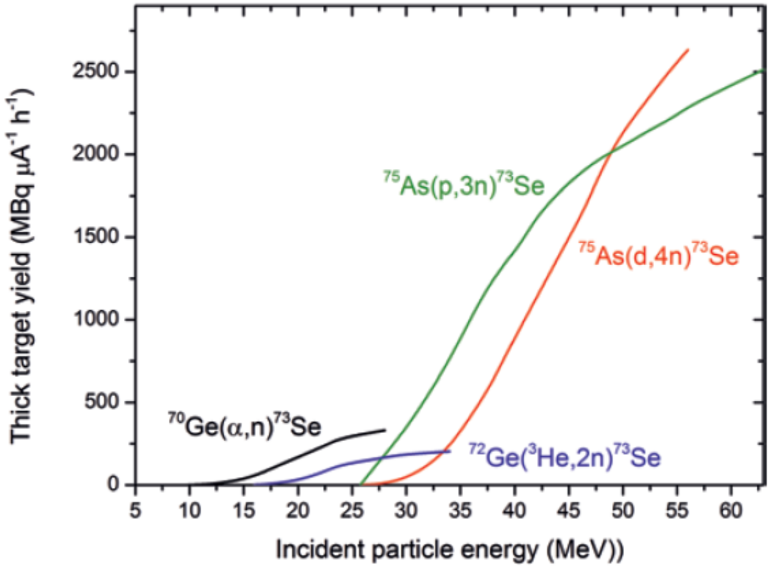
- Boron (natural or 11B) enriched target on silicon substrate
- NB targets

May, a new class of high-power laser-driven α drivers be envisaged for such a goal?

Main advantages/drawbacks of RNs produced by α-beams

- Some RNs may be produced **only via** **α-particle induced reactions;**
- The Z of RNs produced is often +2 **units than the target nuclide →** **chemical separation more specific** and the product can be obtained with very **high radiochemical and chemical purity (mainly for radiometals);**
- The cross sections of some α-induced reaction routes: **(α,xn), (α,p), (α,d), (α,t)** etc. are in general **higher or camparable vs. p/d route , mainly for the light and medium mass target nuclei**.
- **Thick Target Yield (TTY) =** $\frac{N_A H}{M}\frac{I}{Ze}\left(1-e^{-\lambda t}\right)\int_{E_1}^{E_2}\left(\frac{dE}{d(\rho x)}\right)^{-1}\sigma(E)dE$, due to (α,x) nuclear reaction routes are however **lower than those using protons / deuterons**, due to the quite larger α stopping power in materials





The example of the positron-emitter ^{73}Se for PET

Thick target yields of calculated by the excitation functions of

- ^{75}As(p,3n)^{73}Se
- ^{75}As(d,4n)^{73}Se
- ^{72}Ge(3He,2n)^{73}Se
- ^{70}Ge(α,n) ^{73}Se

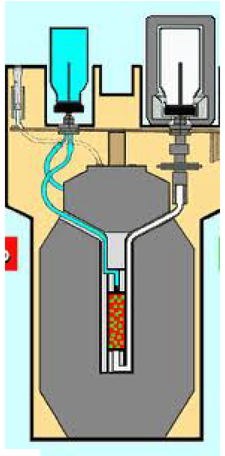
Main issues of RNs produced by α-beams: need of a high intensity source

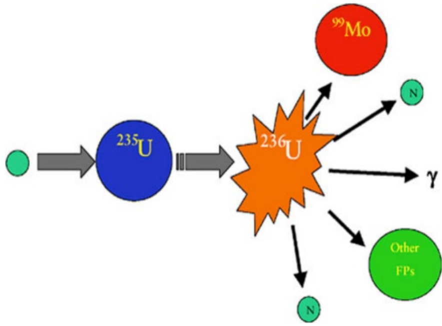
- to get RNs yields comparable to those to produce by p/d beams therefore necessary to improve the α-particle beam-on-target to the order of **500-1000 µA (i.e. ~ 3E+15 - 6E+15 α/s);**
- α-particles may be accelerated **only as positive ions** and the extraction process is more challenging.
- The use of **cyclotron for alpha particles** has an intensity limitation (mainly related to the extraction system) e.g.:
  - The **IBA 70-30 MeV** @ARRONAX (Nantes) is limited **to 35 microA only**
  - The **BCSI 70-35 MeV** @ LNL (SPES/LARAMED) **only allows proton acceleration (optimized)**.
- The new technology now available for linacs DTL (ECRIS Sources), allows, better than cyclotrons, **to supply up to some tens MeV α-particles beams with at least 1 mA intensity.**
- With the availability of high-performance linacs able to drive α beams, **the production routes for well-established as well as emerging RNs may be re-investigated.**
- The **quality of the final product** strongly depends on the chosen target/projectile/energy parameters set (e.g., ^{67}Cu, ^{47}Sc, ^{103}Pd, ^{186}Re, ^{97}Ru and ^{211}At………)

RNs produced by different (p,d, X) routes and corresponding (α, X) ones: Some examples

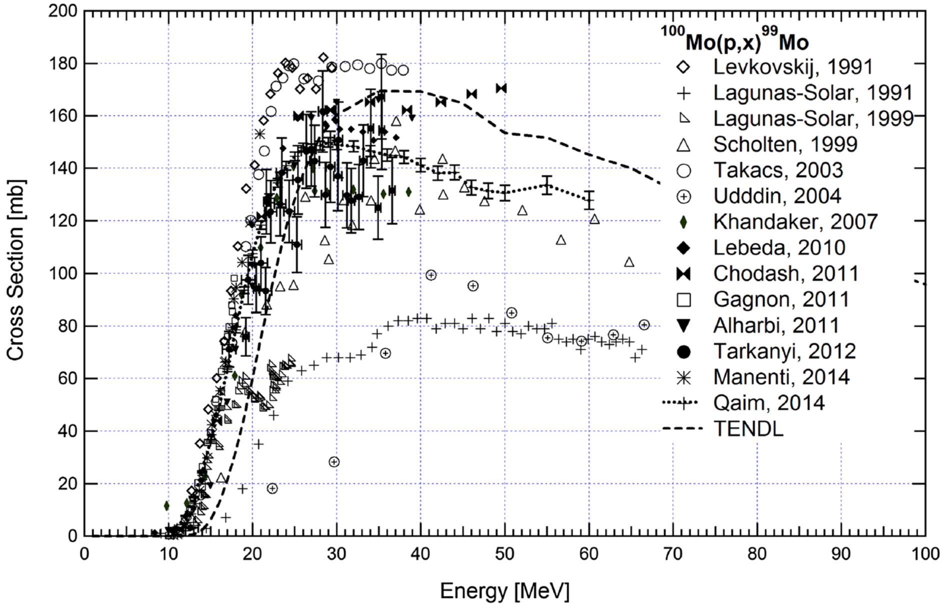
^{99}Mo ->^{99m}Tc generator

(the most used RNs in the world for 50+ yrs allowing SPECT imaging)

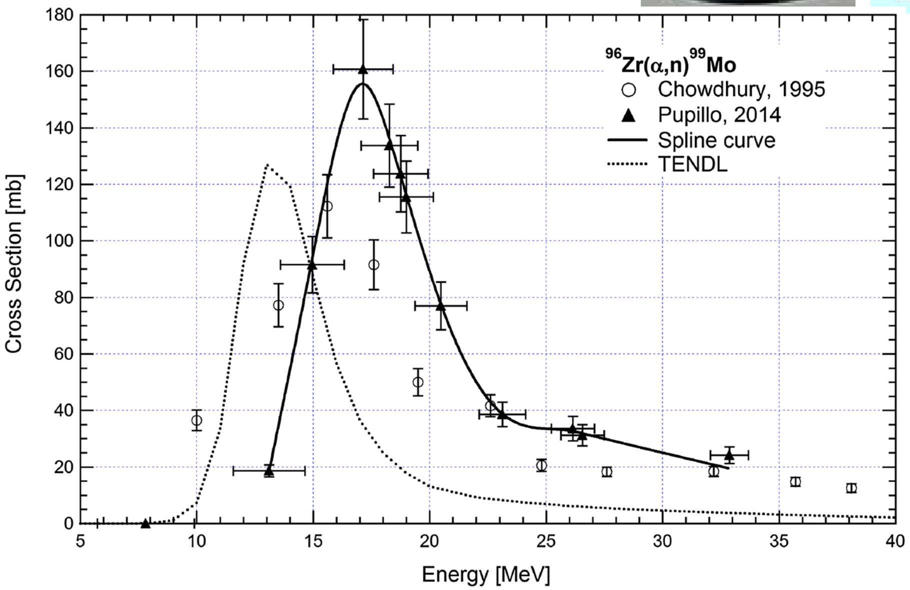




Innovative accelerator-based production routes for ^{99}Mo (and ^{99m}Tc) comparing the **^{100}Mo(p,x)^{99}Mo** and **^{96}Zr(α,n)^{99}Mo** reactions



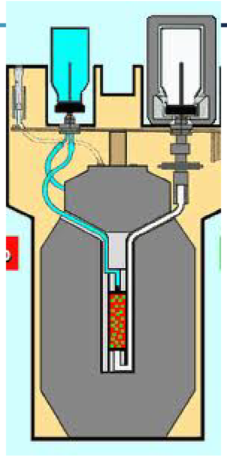
Collection of experimental and theoretical cross section evaluations of the **^{100}Mo(p,x)^{99}Mo** nuclear reaction



Collection of experimental and theoretical cross section evaluations of the **^{96}Zr(α,n)^{99}Mo** nuclear reaction

G.Pupillo, J.Esposito, S.Manenti, F.Haddad, N.Michel, M.Gambaccini, *Accelerator-based production of 99Mo: a comparison between the 100Mo(p,x) and 96Zr(a,n) reactions*, J Radioanal Nucl Chem 305 (10) 2015; 73-78

RNs produced by different (p,d, X) routes and corresponding (α, X) ones: Some examples



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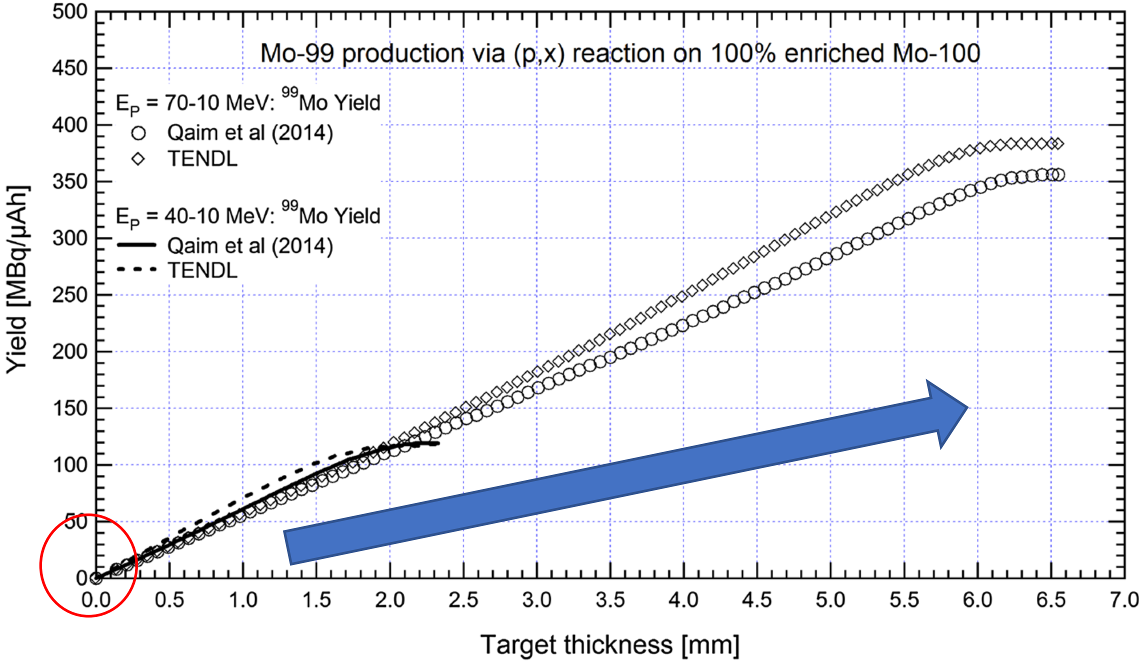
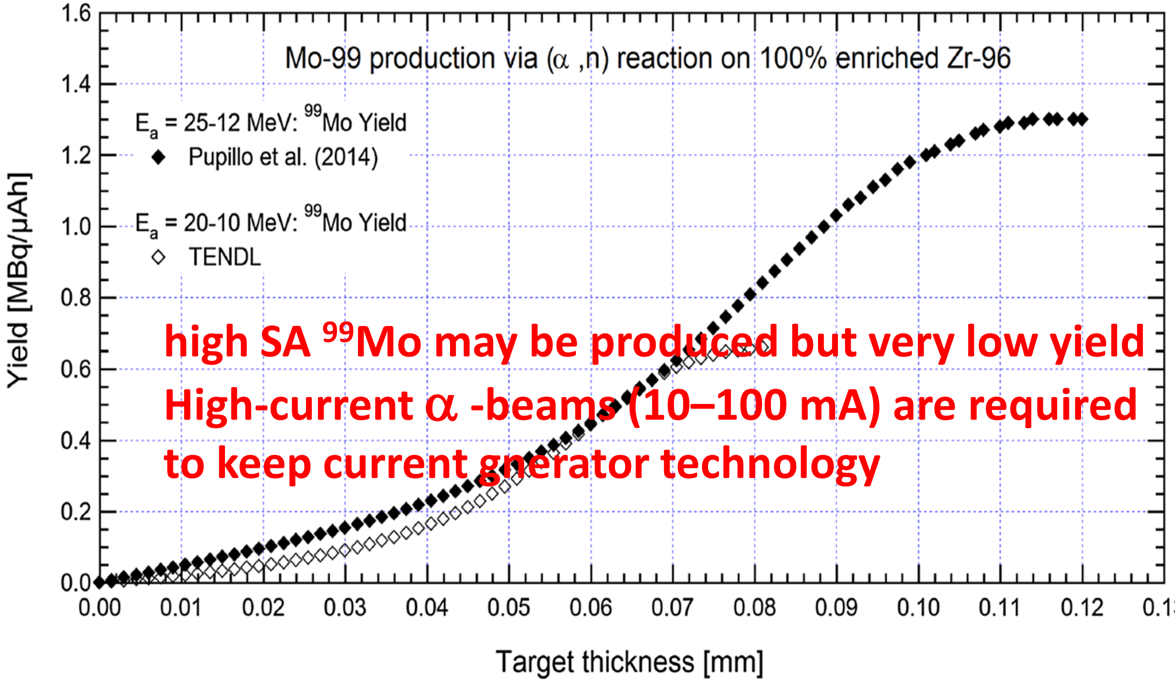
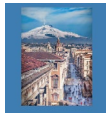
Innovative accelerator-based production routes for ^{99}Mo (and ^{99m}Tc) comparing the **^{100}Mo(p,x)^{99}Mo** and **^{96}Zr(α,n)^{99}Mo** reactions





high SA ^{99}Mo may be produced but very low yield
High-current α -beams (10–100 mA) are required to keep current generator technology



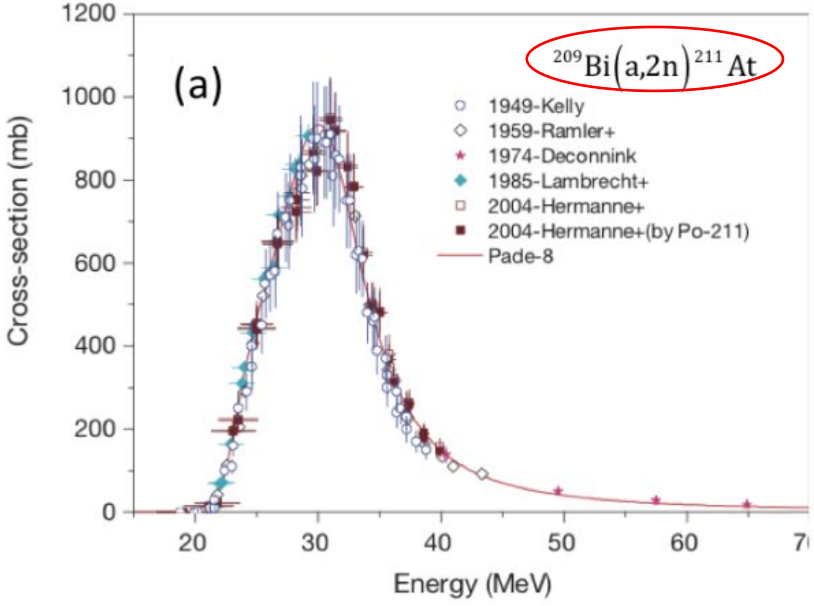
RNs produced by different (p,d, X) routes and corresponding (α, X) ones: Some examples

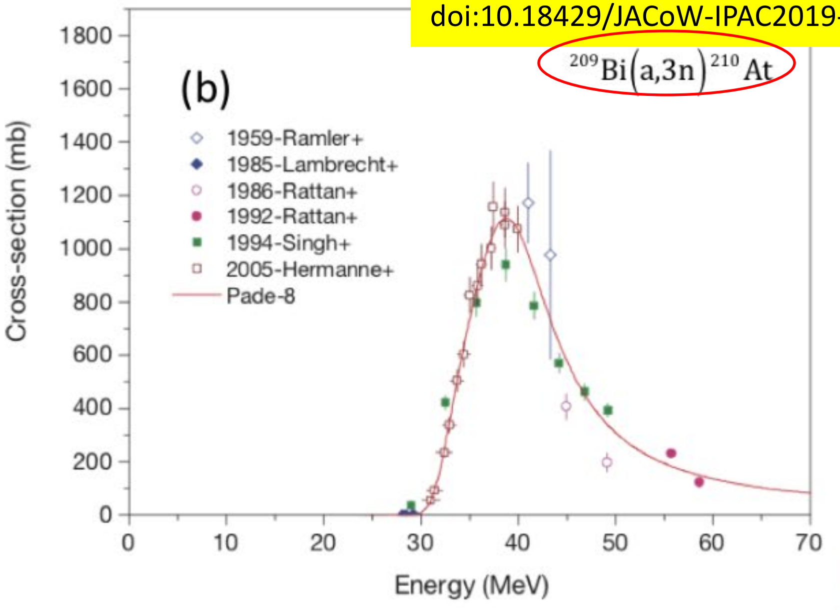
^{211}As ($T_{1/2}$ =7.2 hr) ->α particle emitter (very attractive radioisotope for cancer treatment).

Mainly produced by **^{209}Bi(α,2n)^{211}At route in few GBq quantities**

Major concern: **main contaminant ^{210}At** that has to be minimized due to its decay product Po-210 which is an alpha emitter and binds chemically to the bone marrow

E. J. Prebys∗ , W. H. Casey, D. A. Cebra, R. J Abergel , *Development Of Astatine-211 Production In The Crocker Nuclear Laboratory Cyclotron*, IPAC2019, Melbourne, Australia, doi:10.18429/JACoW-IPAC2019-THPMP051





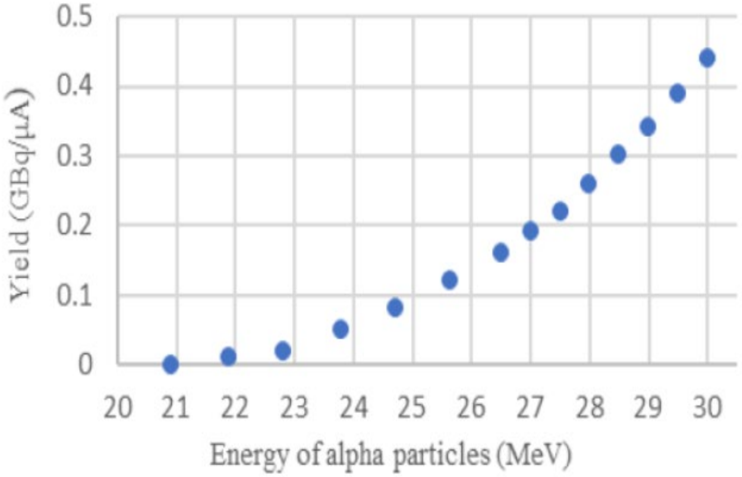
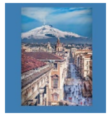


Figure 3: Saturation yield in GBq/μA of ^{211}At, at saturation time of 3.5 $T_{1/2}$≅ 24 h, as a function of $E_{b,alpha}$

Production cross-section as a function of beam energy for (a) ^{209}Bi(𝛼,2n)^{211}At and (b) ^{209}Bi(𝛼,3n)^{210}At.



State of the art and background experience on emerging $^{64/67}$Cu radiometals

Cu-67 ($T_{1/2} \cong$ 62 hrs) **promising radionuclide** for **Theranostic and Radio Immuno Therapy (RIT) applications,** as single isotope, or in pair with ^{64}Cu ($\beta^{+/-}$emitter, $T_{1/2}$ =12.7 h).

- ^{64}Cu is ALREADY used in nuclear medicine for PET diagnostic procedures
- ^{64}Cu seems to provide excellent results also in THERAPY for brain tumors

What will it happen by using ^{67}Cu ?

- ^{67}Cu's limiting factor: Still lacking a **REGULAR availability worldwide**
- Only recently become available in US in enough quantities for **medical research applications (DOE-IP)**
- Production capability upon request **@ ANL-LEAF via ^{68}Zn(γ,p) nuclear reaction (BNL through the ^{68}Zn(p,2p)**
- **→ ^{67}Cu future supply in Europe: Goal both for ARRONAX and LARAMED!!!**

Theranostic = Therapy + Diagnostic

Cu-67	SPECT		THERAPY			
61.83 h	γ-ray [keV]	γ-ray [%]	β energy [keV]	β int [%]	Auger [keV]	Auger [%]
β- : 100 %	184.6	48.7	51	1.1	0.99	19.14
(Zn-67)	209.0	0.115	121	57	7.53	6.87
	300.2	0.797	154	22.0	83.65	12.09
	393.5	0.220	189	20.0	Mean β- : 141 keV	


Drug Discovery Today • Volume 23, Number 8 • April 2018 REVIEWS

ELSEVIER

Teaser Copper radioisotopes are emerging as potent tools for developing unprecedented clinical approaches for cancer treatment by exploiting the intrinsic biological properties of ionic copper and the richness of copper chemistry.

Reviews • KEYNOTE REVIEW

The emerging role of copper-64 radiopharmaceuticals as cancer theranostics

Alessandra Boschi[1], Petra Martini[1], Emilija Janevik-Ivanovska[2] and Adriano Duatti[3]

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Copper radionuclides are rapidly emerging as potential diagnostic and therapeutic tools in oncology, particularly ^{64}Cu-radiopharmaceuticals for targeting neuroendocrine, prostate, and hypoxic tumors. Unexpectedly, experimental results are also revealing the impressive biological behavior of simple [$^{64}Cu^{2+}$] ions. For example, it has been demonstrated that administration of ionic [$^{64}Cu^{2+}$] in physiological solution allows the selective targeting of a variety of malignancies. These remarkable biological properties appear to be crucially linked to the natural role of copper ions in cell proliferation. Here, we review the current status of ^{64}Cu-radiopharmaceuticals in molecular imaging and cancer therapy.

Introduction

Molecular imaging [1–6] is a fascinating concept that has deeply influenced modern diagnostic imaging and therapy. However, its definition is rather vague and does not fully meet the strict requirements of a rigorous scientific concept, resulting in an ongoing lengthy debate. In an attempt to develop a definition that includes its most relevant characteristics, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) proposed the following statement: 'Molecular imaging is the visualization, characterization, and measurement of biological processes at the molecular and cellular levels in humans and other living systems' [6].

Some ambitious interpretation entails that the meaning of the term 'molecular' should be interpreted as the level of spatial resolution that can be attained by methods used for imaging biomolecules in living systems. Only when the same atomic-scale resolution typical of structural chemistry is achieved can the molecular attribute be applied. However, this result is still beyond reach because there is no available imaging technology capable of truly detecting single molecules in living tissues with atomic resolution.

Another interpretation suggests that molecular imaging corresponds to mapping the distribution and activity of molecules in living tissues. This description is linked to the concept of a molecular imaging agent that is defined as a 'probe' used to visualize, characterize, and measure

Alessandra Boschi is currently the head of the Radiation Safety and Control Section at the University of Ferrara and a assistant professor of radiochemistry. Her research interests focus mainly on the development of novel chelating systems for radiometals and the application of radionuclide imaging in preclinical studies.

Petra Martini is currently a postdoc at the Legnaro National Laboratories of the INFN. She is also a researcher fellow at the University of Ferrara. She has also worked at TRIUMF Canada's Particle Accelerator Centre. Her main research interests focus on the production of novel radionuclides for medicine and the development of automated methods for target processing, separation, and purification of radionuclides from cyclotron-irradiated targets.

Emilija Janevik-Ivanovska is currently a professor in pharmaceutical chemistry and technology at the University of Stip. She is also the director of the University Institute for Positron Emission Tomography in Skopje. She is also expert consultant to the International Atomic Energy Agency and the European Directorate for the Quality of Medicines. Her broad research interests range from radiolabeling of peptides and antibodies to the development of molecular imaging agents labeled with positron-emitting radionuclides and radionuclide therapy. She is also involved in various expert committees for the analysis of regulatory aspects related to radiopharmaceuticals.

Adriano Duatti is currently a professor of general and inorganic chemistry at the University of Ferrara and a research associate of the Italian National Institute of Nuclear Physics (INFN). He is Head of the LARAMED project at the INFN Legnaro National Laboratories, which aims develop the production of innovative and nonstandard radionuclides for medical applications using a high-energy (70 MeV) and high-current (800 microA) cyclotron. He is also a radiopharmaceutical consultant to the Italian Ministry of Health. He has also worked at the International Atomic Energy in Vienna, Austria in the Radioisotope Products and Radiation Technology Section. His main research interests focus on the chemistry of metallic radiopharmaceuticals, molecular imaging, and targeted radionuclide therapy.

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https://doi.org/10.1016/j.drudis.2018.04.002

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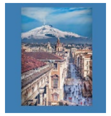


RNs produced by different (p,d, X) routes and corresponding (α, X) beams: Some examples

^{67}Cu ($T_{1/2}$ =61.83 hr) -> β^- /γ decay (under the spotlight of international community. May be used both for therapy and associated diagnostic applications. A very promising theranostic radionuclide.

Produced in almost pure form (but limited amount) with the **^{70}Zn(p,α)^{67}Cu or ^{70}Zn(d,α)^{67}Cu in selected energy ranges by p/d beams. An alternative interesting route is ^{64}Ni(α,p)^{67}Cu on highly enriched (>99%) ^{64}Ni targets**

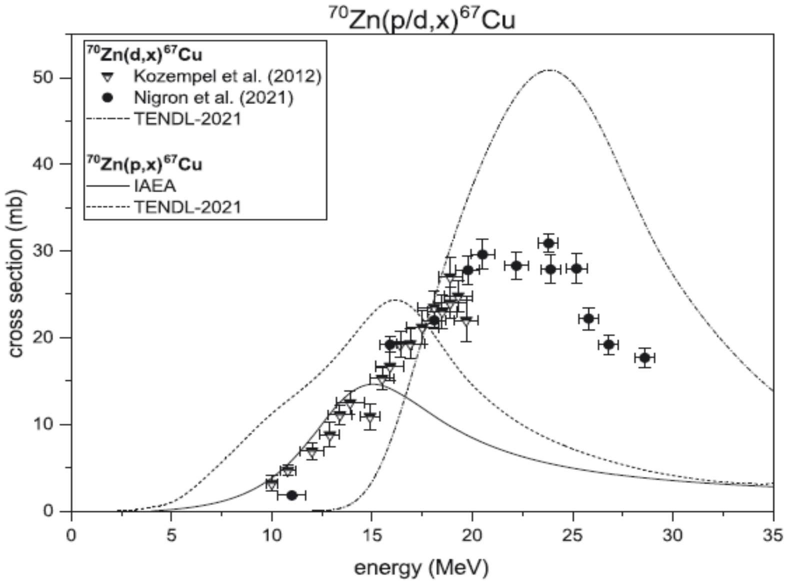


Figure 2: ^{67}Cu production cross sections induced by deuteron and proton beams on ^{70}Zn targets.

Table 2: ^{67}Cu and ^{64}Cu production yields obtained by using proton, deuteron and α-beams on ^{70}Zn, ^{68}Zn, and ^{64}Ni enriched target materials assuming I = 30 μA and T_{Irr} = 24 h.

Beam	Target	Energy range (MeV)	Thickness (mm)	^{67}Cu at EOB (GBq)	^{64}Cu at EOB (GBq)
Protons	^{70}Zn	25–10	1.22	3.0	–
	^{68}Zn	70–35	6.43	17.5	150
	^{70}Zn	68–45	4.61	22.2	140
Deuterons	^{70}Zn	26–13	0.68	4.3	–
Alpha	^{64}Ni	30–0	0.15	1.0	–

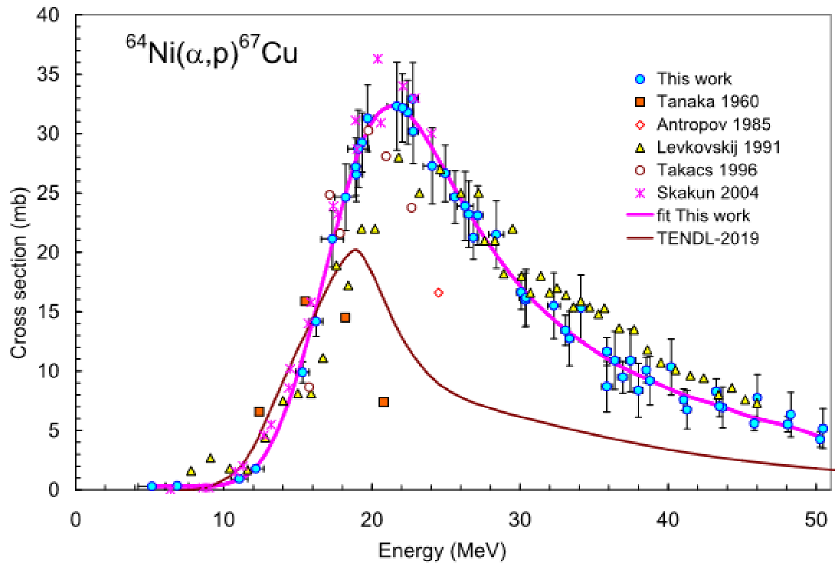
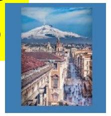


Fig 4. Experimental cross sections of the 64Ni(α,p)67Cu reaction in comparison with the earlier experimental works.

G.Pupillo, S. Manenti, F.Groppi, J.Esposito, F.Haddad, *Nuclear data for light charged particle induced production of emerging medical radionuclides*, Radiochim. Acta 2022; 110(6–9): 689–706

S.Takácsa, M.Aikawab, H.Habac, Y.Komoric, F.Ditrói Z. Szűcs, M.Saito, T. Murata, M. Sakaguchi, N. Ukona, *Cross sections of alpha-particle induced reactions on natNi: Production of 67Cu,* Nucl. Inst. Meth 479 (2020) 125-136.



RNs commonly produced by (α, X) reaction routes

Table 1: Radionuclides commonly produced using the α-particle beam.

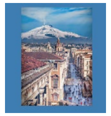
Radio-nuclide	$T_{1/2}$	Radiation emitted (%)	Nuclear reaction	Energy range (MeV)	Yield[a)] (MBq/μAh)	Purity (%)	References to production	Other investigated reactions[e)] [Reference]
^{28}Mg	21.1 h	β^- (100)	^{27}Al(α,3p)^{28}Mg	140 → 30	1.5	> 99	[56, 57]	^{26}Mg(t,p)^{28}Mg (cf. [56, 57])
^{30}P	2.5 min	β^+ (100)	^{27}Al(α,n)^{30}P	24 → 10	ca. 1000[b)]	> 99.9	[60, 61]	^{32}S(n,t)^{30}P [61]
^{38}K	7.6 min	β^+ (100)	^{35}Cl(α,n)^{38}K	22 → 7	ca. 400[b)]	> 99.8	[62–67]	^{38}Ar(p,n)^{38}K [68] ^{40}Ar(p,3n)^{38}K [69, 70]
^{43}K	22.2 h	β^- (100)	^{40}Ar(α,p)^{43}K	21 → 10	7.0	97.5	[74–76]	^{44}Ca(γ,p)^{43}K [77, 78] ^{43}Ca(n,p)^{43}K [79]
^{77}Br	57.0 h	EC (99.3) β^+ (0.7)	^{75}As(α,2n)^{77}Br	28 → 16	16.6	> 99.9	[84–87]	^{77}Se(p,n)^{77}Br [88, 89] ^{78}Se(p,2n)^{77}Br [89, 90] ^{79}Br(p,3n)^{77}Kr → ^{77}Br [91, 92] ^{79}Br(d,4n)^{77}Kr → ^{77}Br [93]
^{95}Ru	1.65 h	EC (85.0) β^+ (15.0)	^{92}Mo(α,n)^{95}Ru	28 → 14	240[c)]	> 99	[97, 98]	^{nat}Mo(^{3}He,xn)^{95}Ru [97, 98]
^{97}Ru	2.9 d	EC (100)	^{nat}Mo(α,xn)^{97}Ru	28 → 16	1.8[d)]	> 99.8	[97–99]	^{nat}Mo(^{3}He,xn)^{97}Ru [97, 98]
^{147}Gd	38.1 h	EC (99.7) β^+ (0.3)	^{144}Sm(α,n) ^{147}Gd	27 → 12	4.8	> 99.8	[100, 101]	^{147}Sm(^{3}He,3n)^{147}Gd [100, 101]
^{211}At	7.3 h	EC (58) α (42)	^{209}Bi(α,2n)^{211}At	28 → 10	17.5	> 99	[81, 104–110]	^{232}Th,^{238}U(p,spall)^{211}At [112] ^{209}Bi(^{6,7}Li,xn)^{211}Rn → ^{211}At [113, 114]

a) Calculated from excitation function.
b) This is saturation yield.
c) Value extrapolated to 100% enrichment of ^{92}Mo.
d) At 15 h after EOB.
e) For comments on these reactions, see text.

….and other interesting RNs for NM applications produced by different (p,d, X) routes may be explored by corresponding (α, X) beams….

Table taken from:

S. Qaim et al., *Uses of alpha Particles, especially in Nuclear Reaction studies and Medical Radionuclide Production,* Radiochim. Acta 2016; 104(9): 601–624



Conclusion and future perspectives

- A great deal of radionuclides for NM applications is currently produced, on a routine basis, by using proton beams, both for imaging (PET/SPECT) and therapy.

- Many interesting radionuclides may be produced by **exploiting (α, X) nuclear reaction routes**, which allow in many cases both **radionuclidic and radiochemical purities levels unattainable with more conventional processes (protons).**

- This production process is currently limited by the availability of **intense enough accelerated alpha beams.**

- However new technologies are now at the frontier: **the high intensity (i.e. up to ~ 1 mAe, 6E15 s^{-1}), energy modulated (4-10 MeV/u) alpha-DTL** under study at INFN-LNL.

- **The challenge:** high-intensity alpha sources, driven by the **p(11B, α)8Be – in short p-11B ->3α reaction** and triggered by high-power laser systems, with enough repetition rate to avoid solid target pulsed thermal stresses, may become in the near term **a new class of α drivers to be employed for such a goal?**

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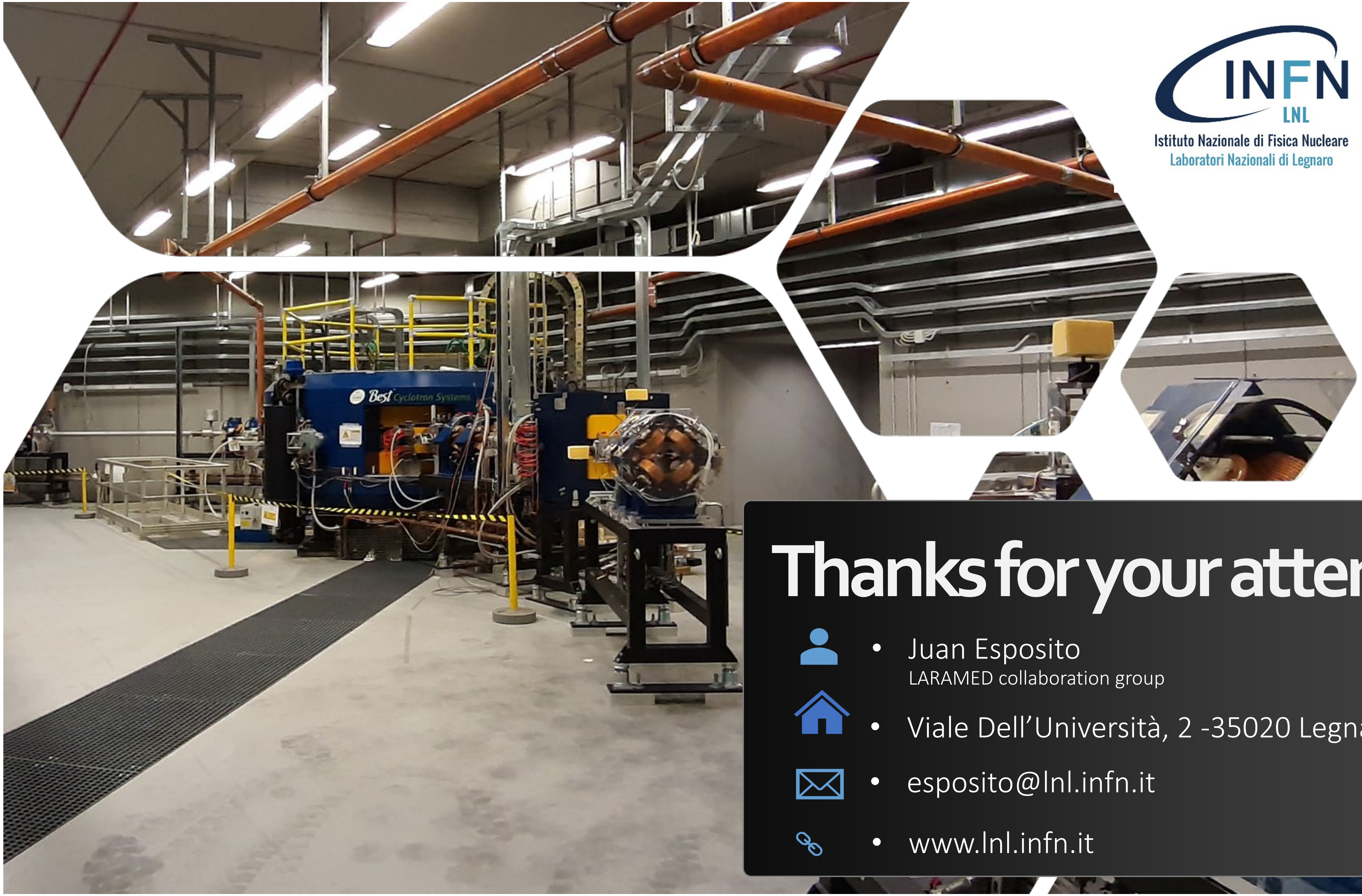

Thanks for your attention

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