Radioisotope production and industrial applications

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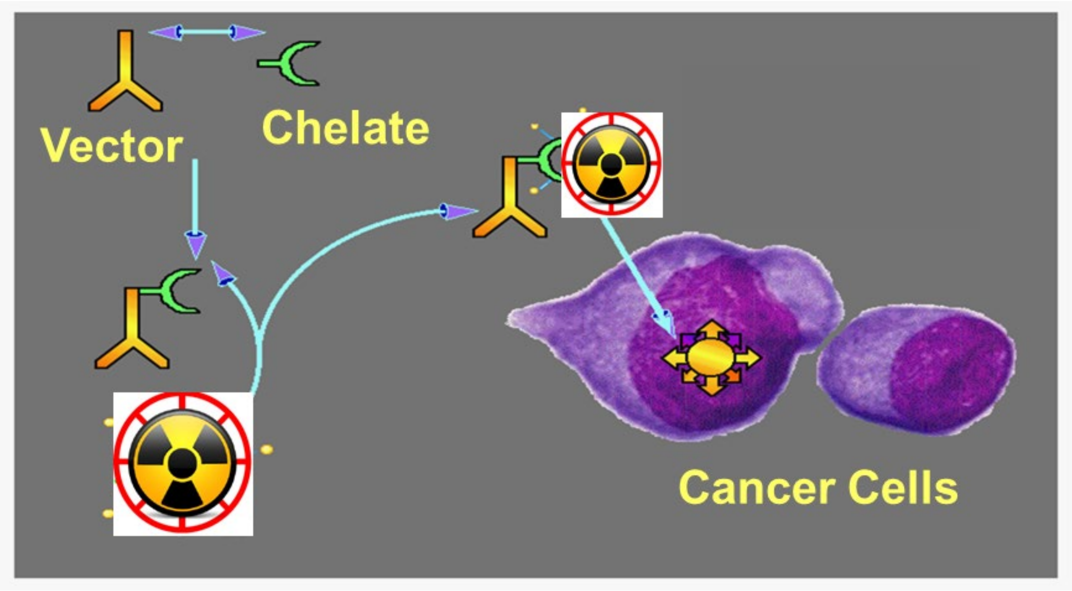
Radionuclides production for nuclear medicine

In Nuclear medicine, radionuclides are used:

- for **imaging and diagnosis** (X-ray, γ , β+)
- for **therapy** (α, β-, Auger-e)

In most cases, **a vector molecule is needed** to target the cells of interest.

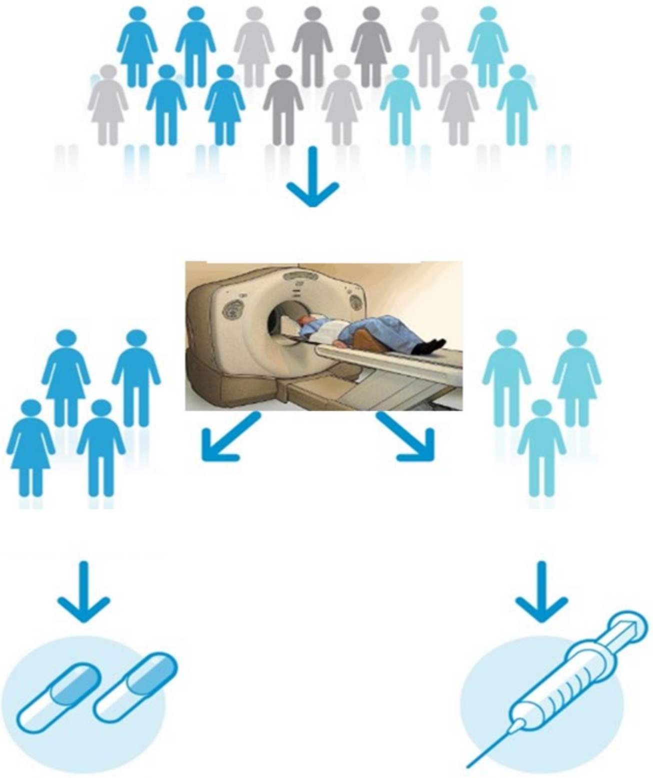


We need to **adapt $T_{1/2}$** to the distribution time of the vector molecule

Theranostics

It is a **treatment strategy** that combines **thera**peutics with diag**nostics**.

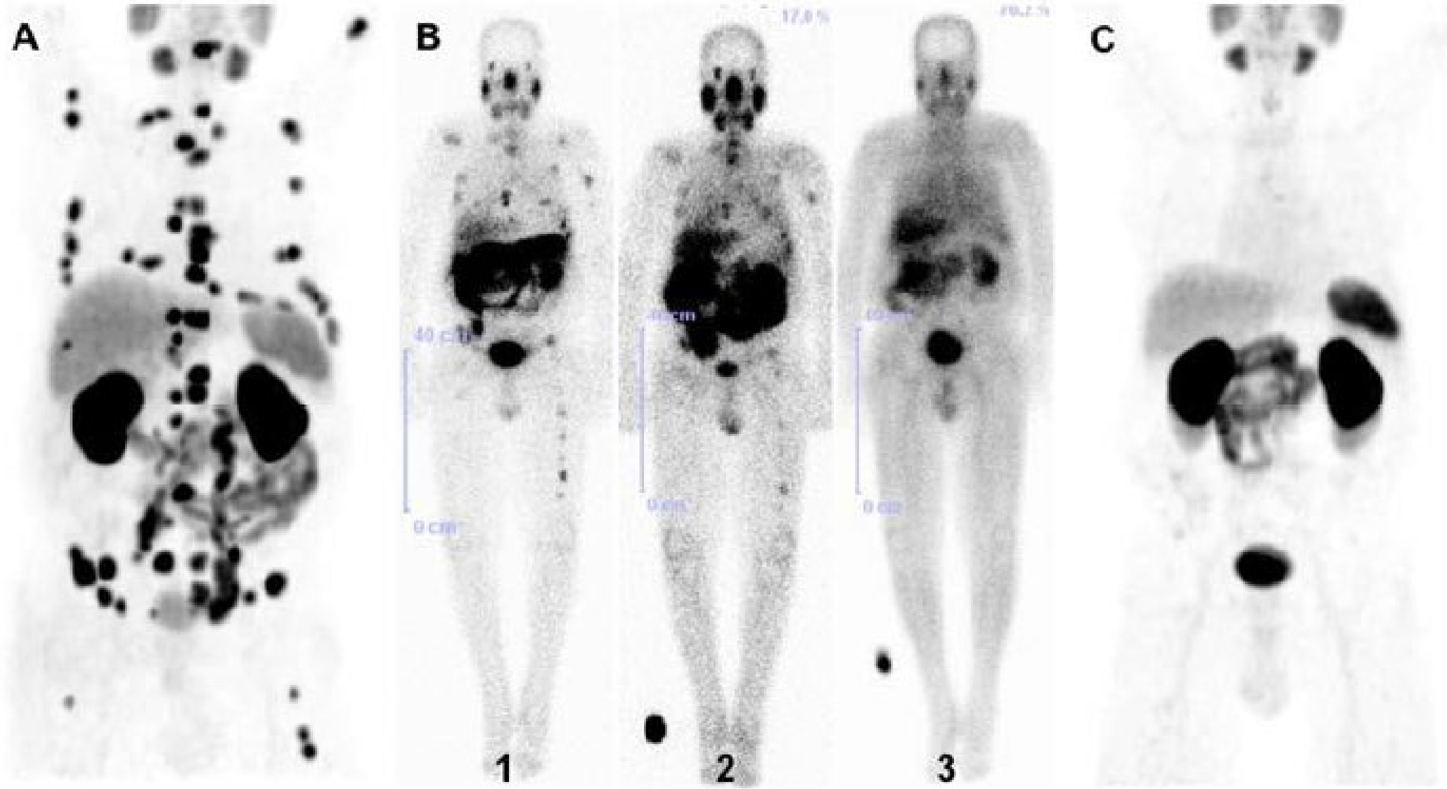
- Localized lesions
- Define the **biodistribution** of a therapeutic agent to anticipate its effect
- **Select patients which are expected to response to the therapeutic agent**
- Calculate the optimal activity to be injected
- Evaluate the response after treatment



The Right Drug To The Right Patient For The Right Disease At The Right Time With The Right Dosage

Targeted internal radiotherapy

^{177}Lu-radioligand therapy of advanced prostate cancer



R.P. Baum et al., J Nucl Med 2016;57:1006.
C. Kratochwil et al., J Nucl Med 2016;57:1170.
K. Rahbar et al., J Nucl Med 2017;58:85.

Activity injeced to patient:
~7,4GBq

There is a demand for new radionuclides

- with different **decay radiations** (imaging / therapy – High LET vs Low LET)
- with different **Chemical properties**
- with different **Half-lives:** to match with vector distribution time in targeted therapy
- To be used for the **Theranostics approach**

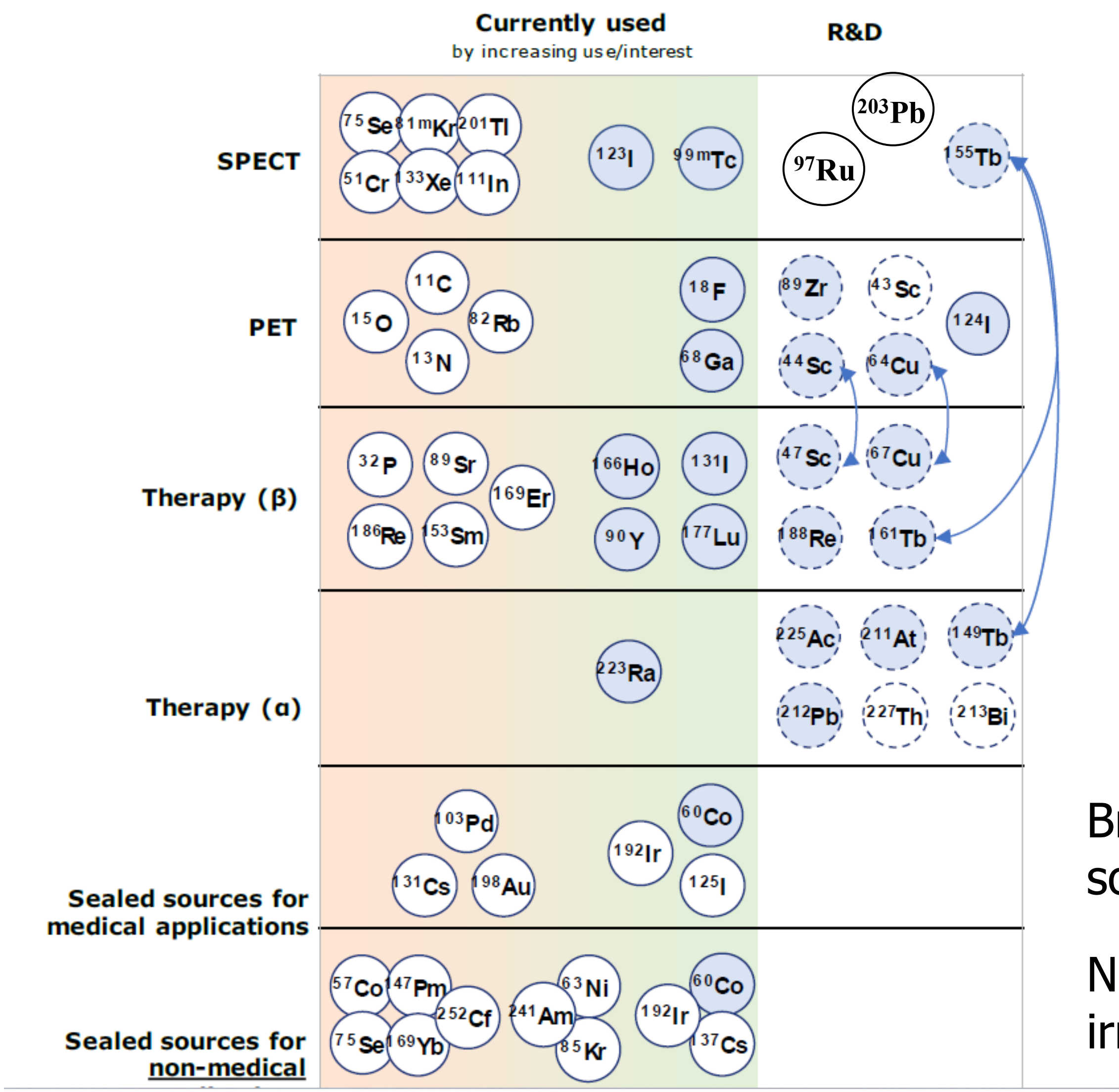
Over the last years, several radionuclides have emerged:

- **β^+:** ^{64}Cu, ^{68}Ga, ^{89}Zr …
- **γ:** ^{203}Pb, ^{97}Ru …
- **β^-:** ^{166}Ho, ^{177}Lu …
- α: ^{211}At, ^{212}Bi, ^{213}Bi, ^{223}Ra, ^{225}Ac ...
- **Auger**: ^{117m}Sn, ^{155}Tb, …
- **Theranostic**: ^{44}Sc/^{47}Sc, ^{64}Cu/^{67}Cu, ^{68}Ga/^{177}Lu …

Existing medical products :

- Diagnosis (γ, β^+) : ^{99m}Tc, ^{18}F, ***Detecnet (^{64}Cu)***
- Therapy (β^-, α, e_{Auger}) : ^{131}I, ^{90}Sr, ***Pluvicto(^{177}Lu), Lutathera (^{177}Lu)***

There is a need for radionuclides



Brachytherapy, gamma source …

Neutron sources, gamma irradiation,…

Adapted from « co-ordinated Approach to Development and supply of radionuclides in the EU » N°ENER/D3/2019-231

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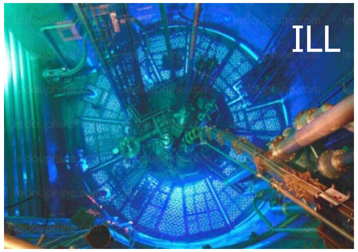
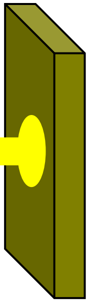
Radionuclide production scheme

Nuclear reactor



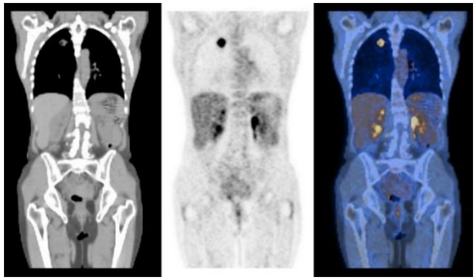
Particle accelerator

production

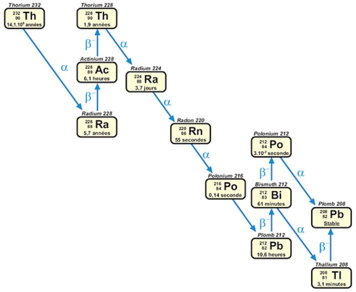


Extraction/
purification

Radio
labeling

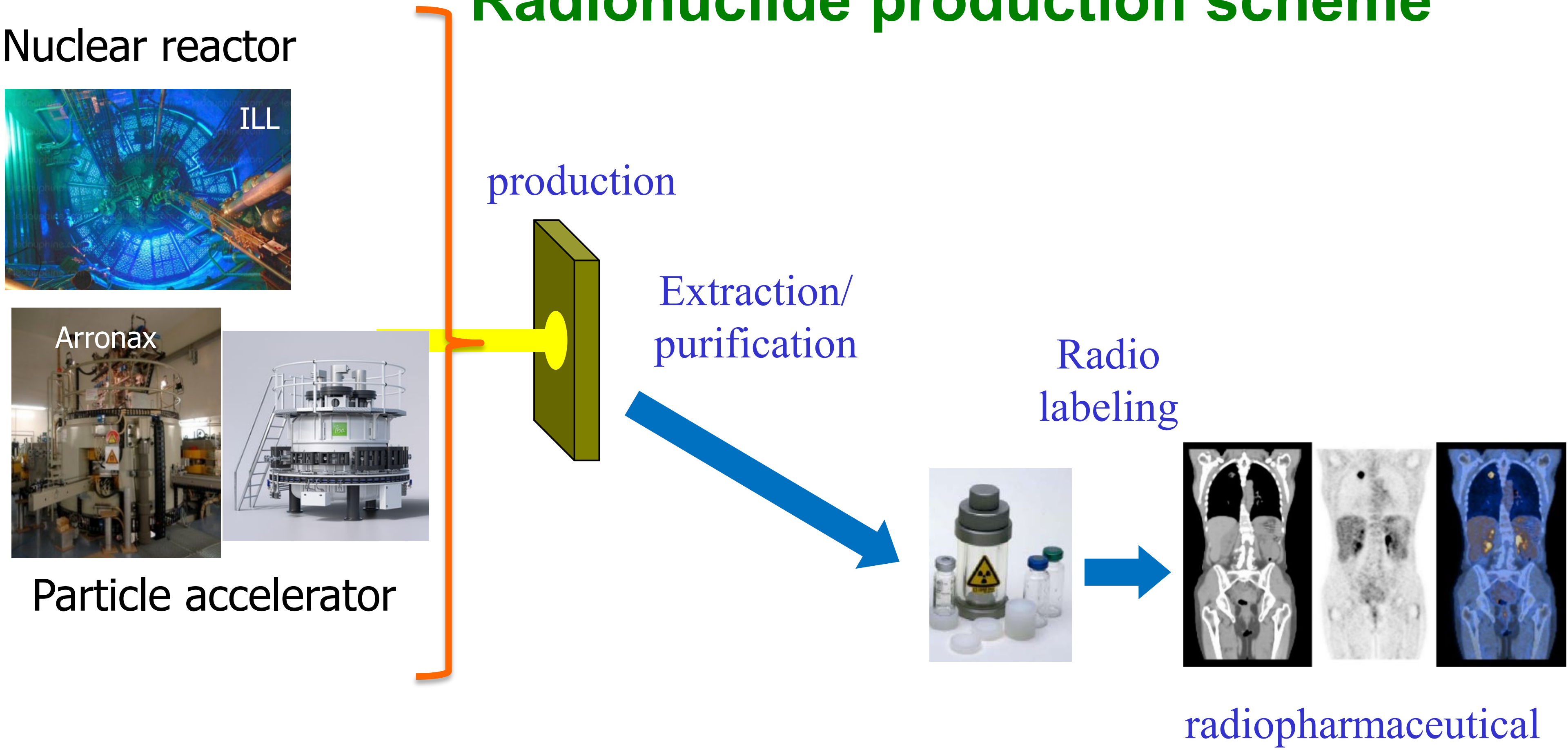


radiopharmaceutical



From decay chain
of heavy nuclei

Radionuclide production scheme



How to optimize production yields ?

Irradiation conditions

Cross section

Produced activity (Bq)

$$Act = \Phi \cdot \chi \cdot \frac{Na.\,\rho}{A} \cdot \left(1 - \exp(-\lambda . t_{irr})\right) \cdot \int_{E_{fin.}}^{E_{in.}} \frac{\sigma(E)}{\frac{dE}{dx}} \cdot dE$$

Target properties

Radioactive decay

To have an impact in nuclear medicine, it is mandatory to consider:

- Irradiating at **high beam intensity** (>100µA)
- Using **thick targets**
- using **enriched material** to limit impurities and increase yields
- **Recycling** target material to reduce costs

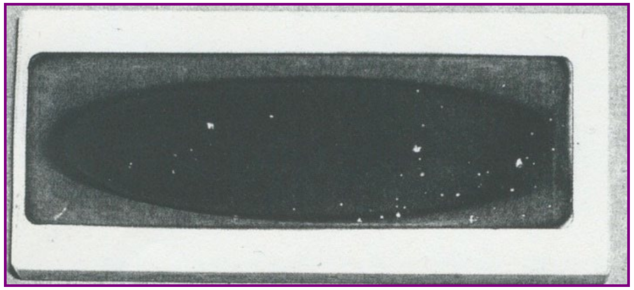
Most target material are stable element (or long lived radioactive element as for example ^{226}Ra or ^{232}Th to produce ^{225}Ac)

Enriched material mostly from Russia

Target for isotope production

- Target can have **different nature** (liquid, gas, solid) and **different Chemical form** (Rb metal or RbCl)
- **Target geometry** is **machine specific** linked to the cooling system, the window material, the target backing material or container material etc …
- **Different technique** can be used to fabricate target (electroplating, evaporation under vacuum, pressed pellets, liquid target in container, …)
- **Target characteristics** are of great importance: uniformity of the target, homogeneity, thickness, thermal and mechanical characteristics …
- **Anticipate impact** on high intensity irradiation, handling, radioprotection, purification chemistry, final isotope purity, quality assurance, waste production, cost, recycling, …

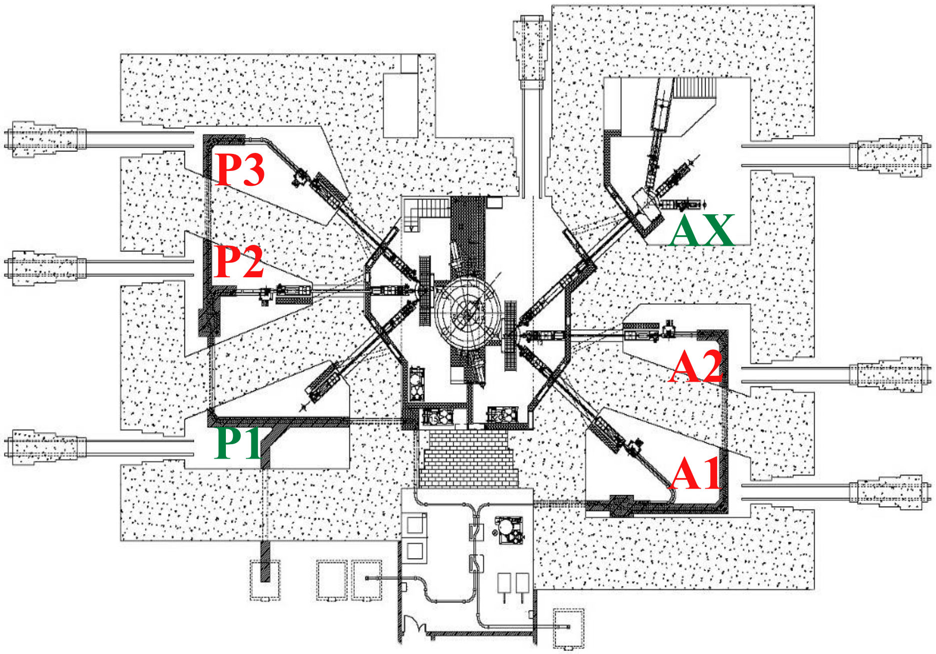
^{64}Ni electroplating on Au backing



Bi deposition under vacuum on Al backing

RbCl pellet before (left) and after (right) encapsulation

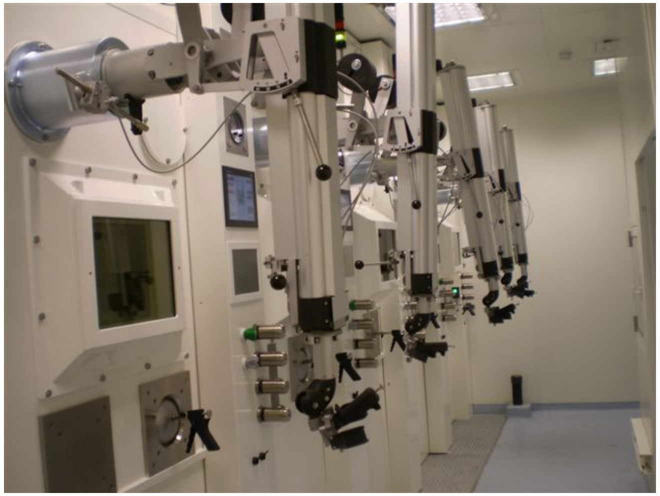
ARRONAX: the facility



4 Vaults devoted to isotope production and connected to ***hot cells*** through a **pneumatic system**

Vault **P1** to accommodate soon a 18 MeV accelerator for ^{64}Cu production

Vault **AX** devoted to physics, radiolysis and radiobiology experiments



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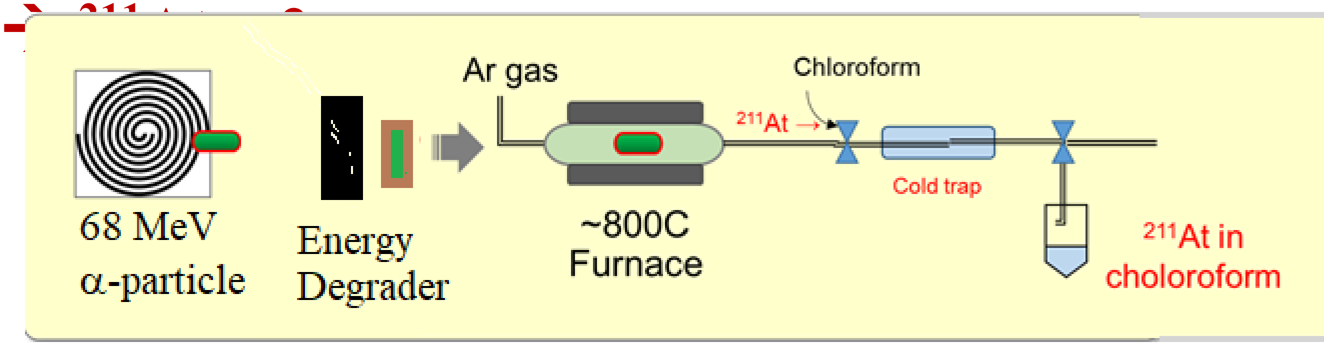
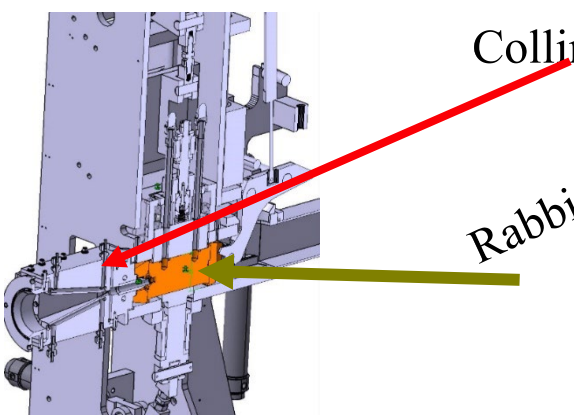
^{211}At: Production à ARRONAX

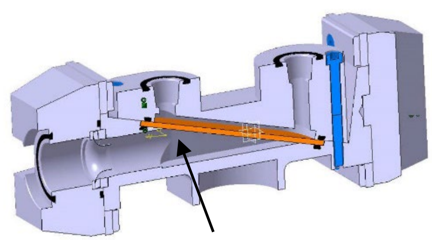
Astatine-211 production route: (activity injected to patient : up to 740 MBq)

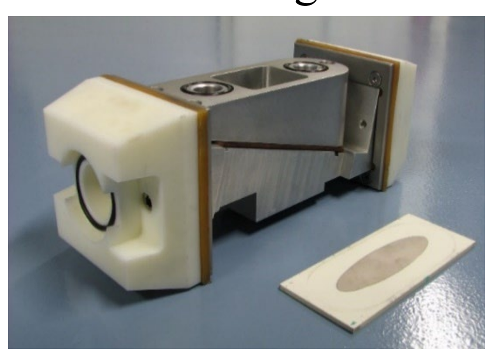
$^{209}Bi + \alpha \rightarrow$

Production scheme @Arronax :

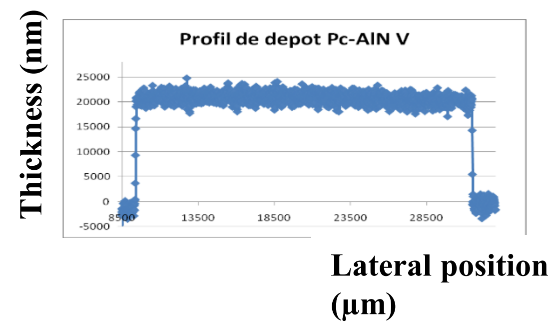


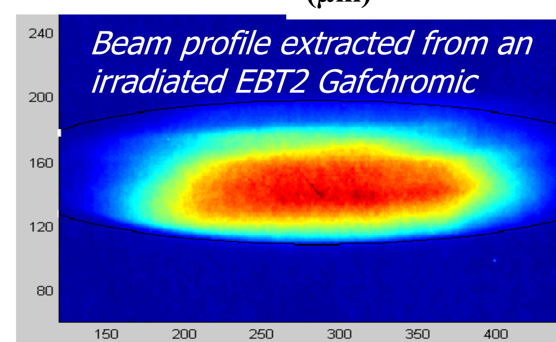




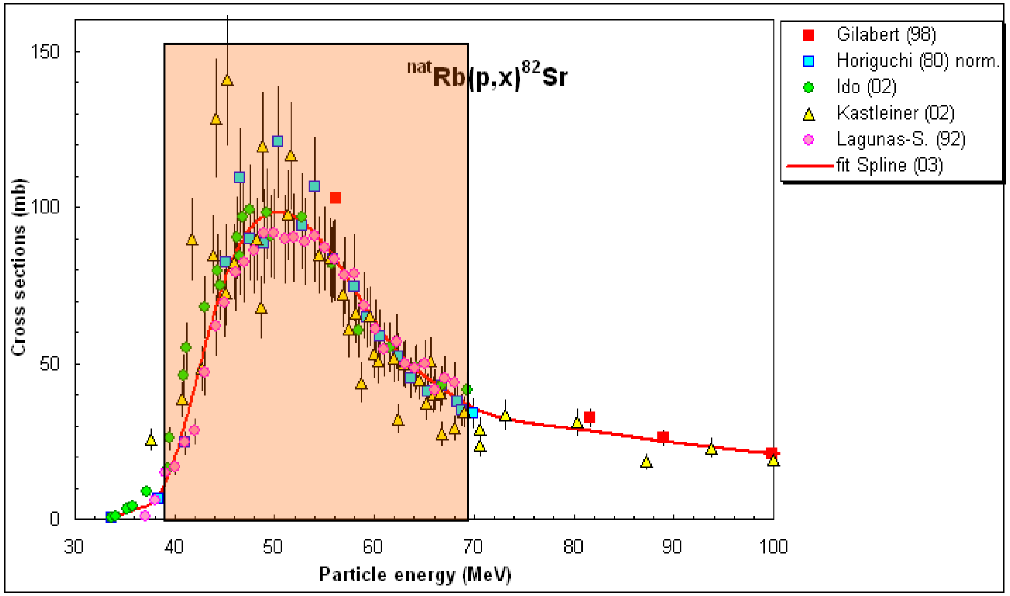


The IBA rabbit system (left) and a target for astatine production (right) to be used at ARRONAX.





^{82}Sr production ($p + {}^{nat}Rb \rightarrow {}^{82}Sr + xn$)

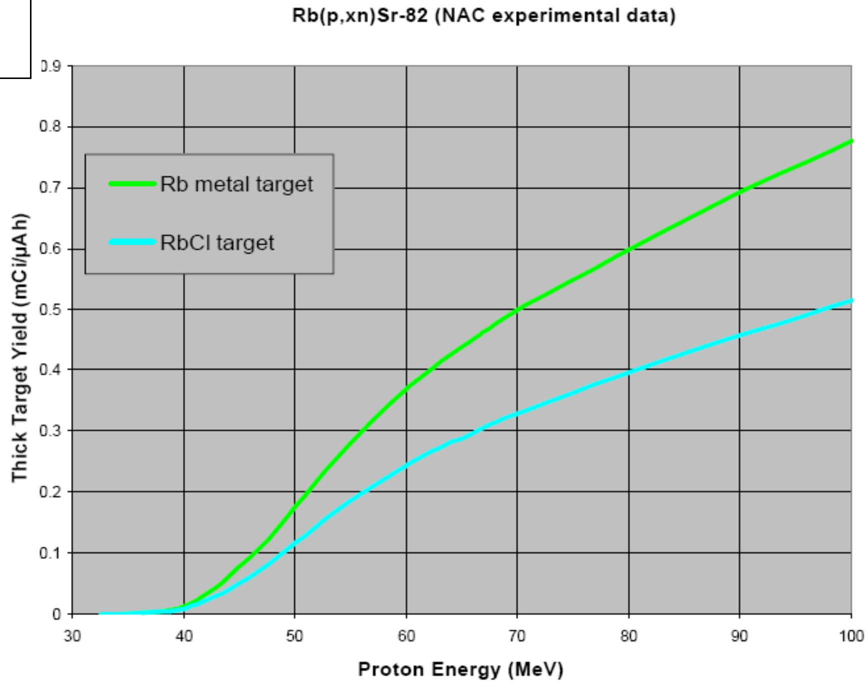


High energy required

Low cross section

→ high intensity required (>100 µA on target)

→ Thick target required (>few mm)



Target must contains Rb as:

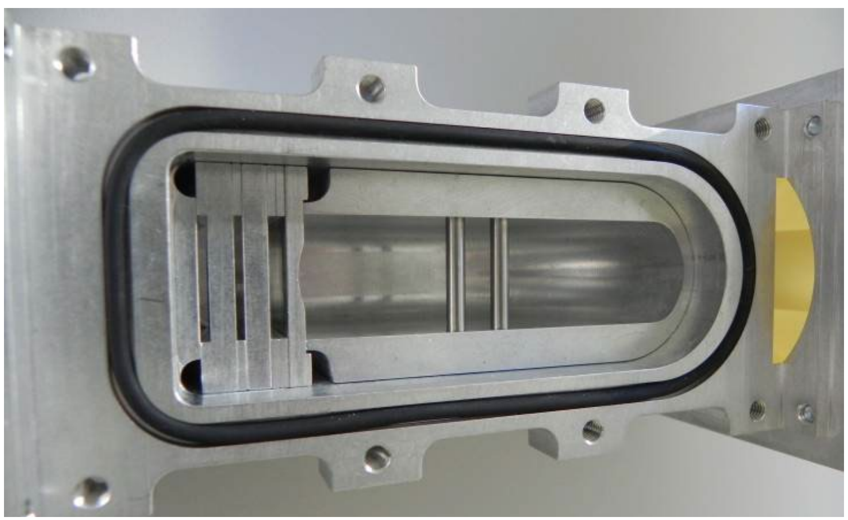
→ RbCl (lower yield but lower risk)

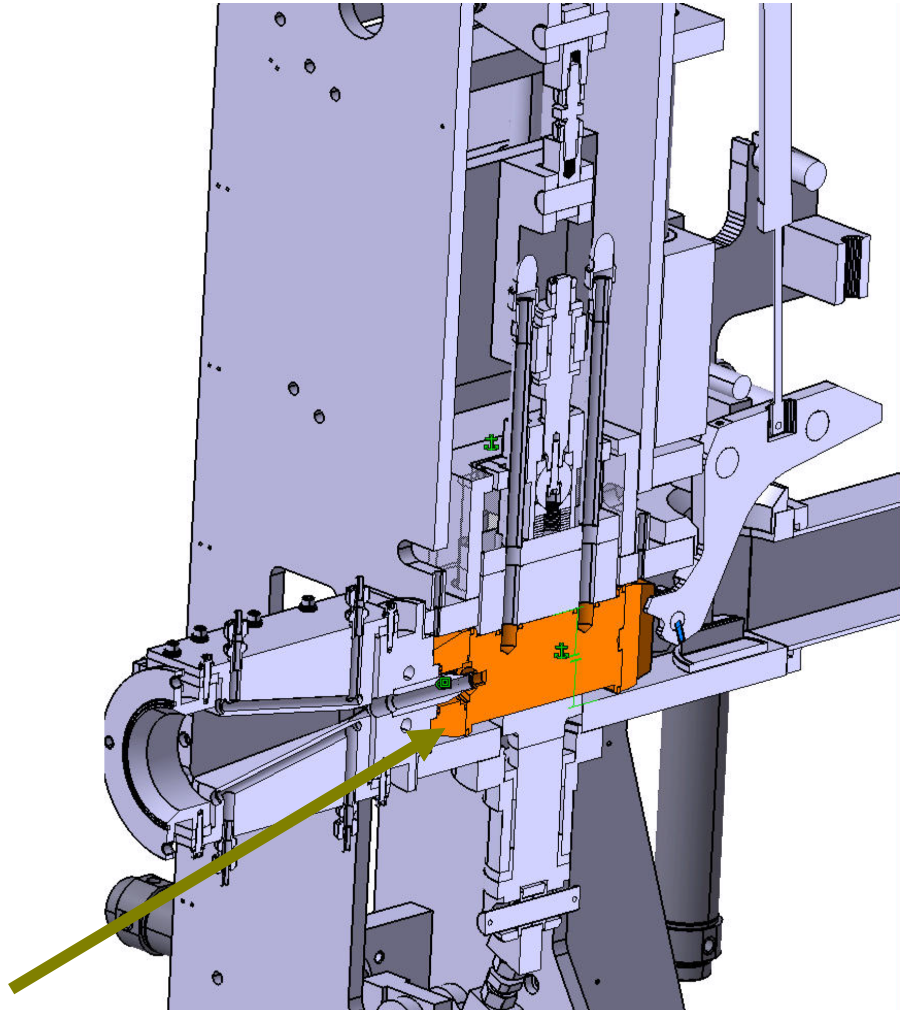
→ Rb metal (higher yield but high risk – alkalin)

RbCl target for ^{82}Sr production

RbCl pellet (4mm thick)

RbCl encapsulated

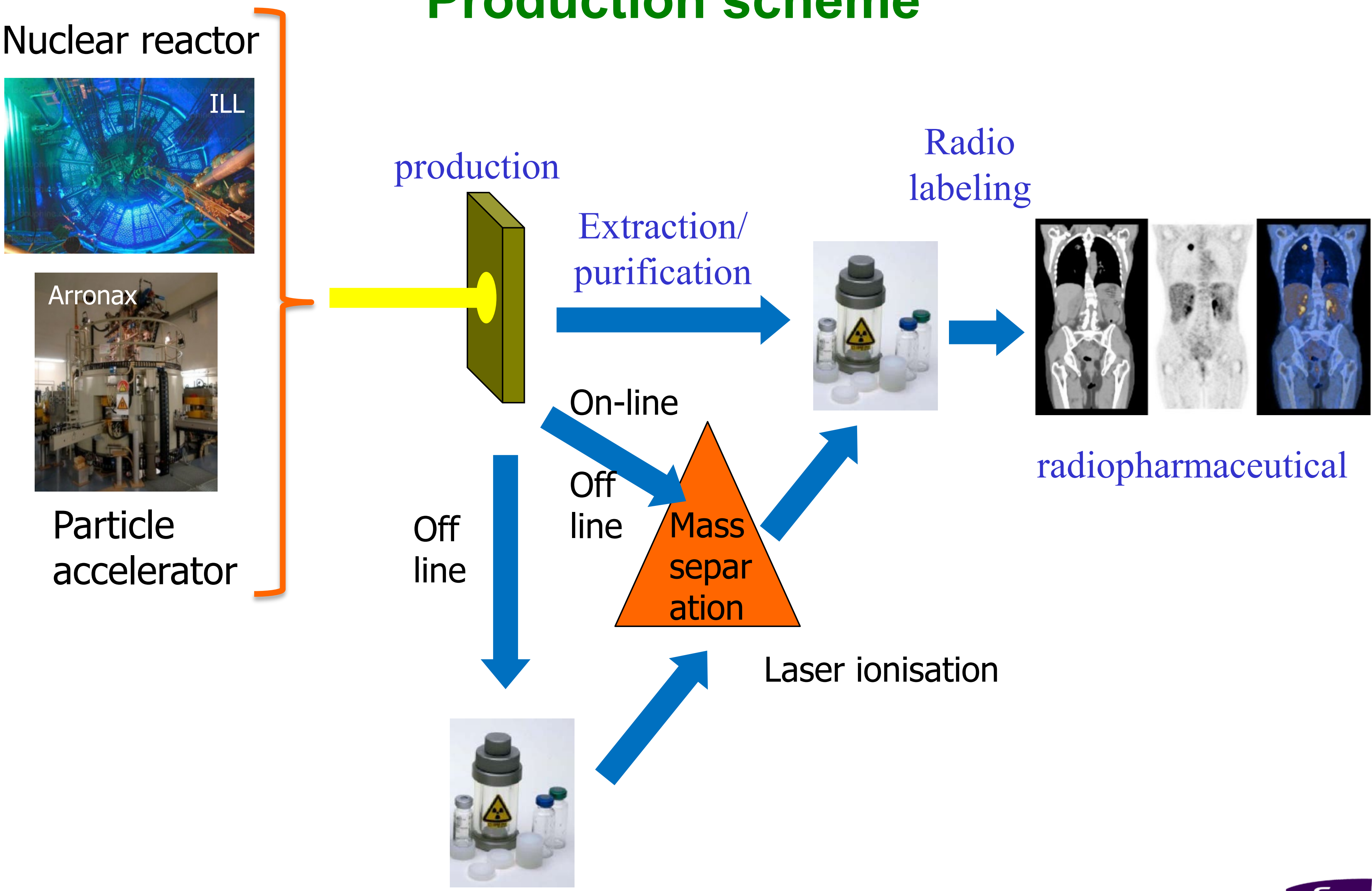




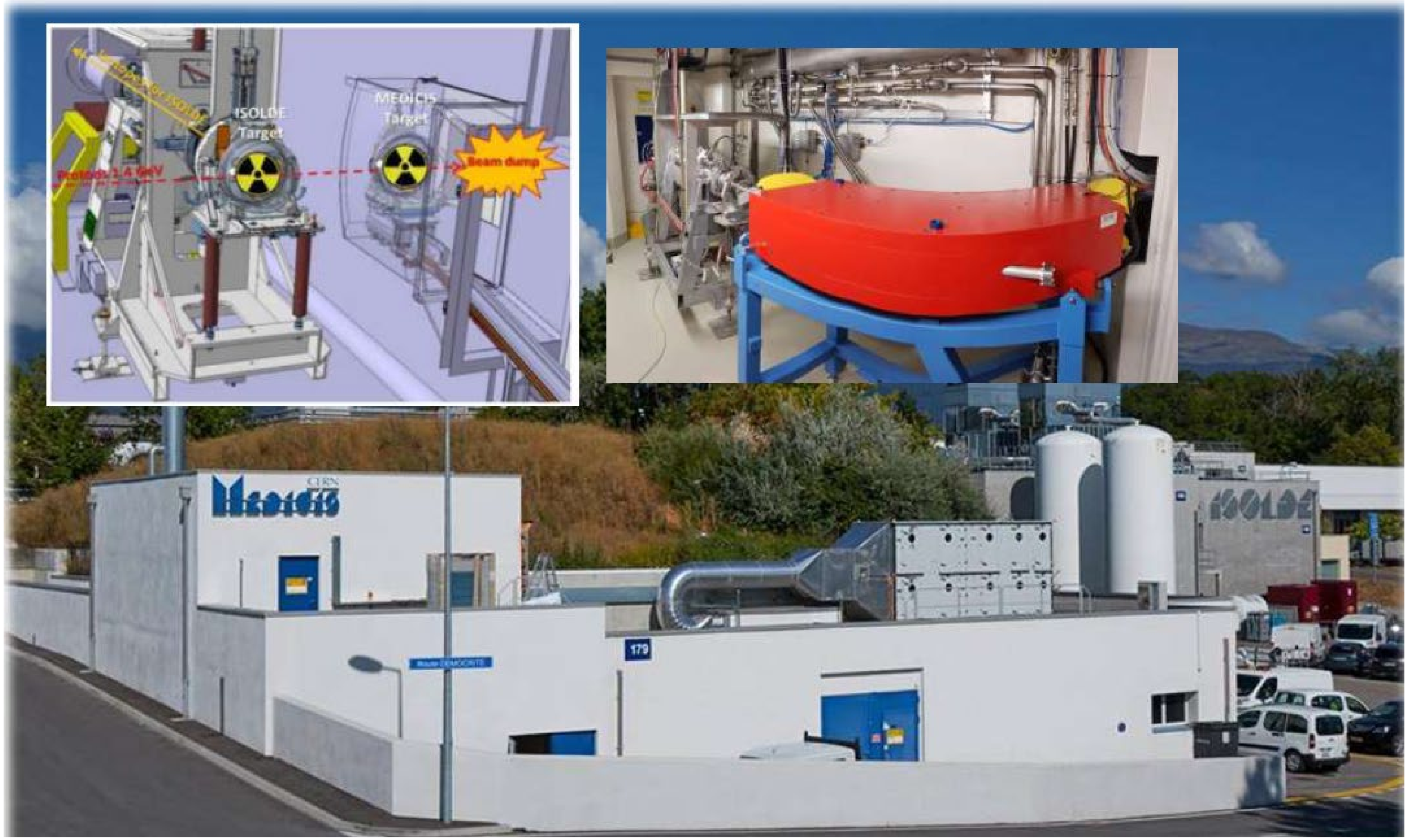
Rabbit

Al window to allow 4pi cooling on targets - 2 targets irradiated in a given rabbit - Dual beams irradiation possible

Production scheme



a very useful beam dump !



Medicis can also accomodate material irradiated elsewhere : ILL, SCK-CEN, Arronax, PSI …

Conclusions

General comments:

- There is an increase need of radionuclides both in therapy and imaging
- There is always several possible production route for a given radionuclide
- The product final purity is a key parameter and may differ from one production route to another
- **Regular quantitative production** is required for applications
- It is very important to anticipate the possible consequences of a target design to other production steps

Solid Targets:

- Many radionuclides can be produced using solid target solutions.
- Solid target system are now available for biomedical cyclotron.
- Production yield for solid target is higher than liquid target (cf. ^{68}G**a)**
- Enriched material is often required
- Recycling is important.

Thank you for your attention

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