UNIVERSITÀ DEGLI STUDI DI MILANO

INFN
Istituto Nazionale di Fisica Nucleare

La produzione di radionuclidi per applicazioni in medicina

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UNIVERSITA' DEGLI STUDI DI MILANO BICOCCA

Fondazione di Comunità MILANO
CITTÀ, SUD OVEST, SUD EST, MARTESANA

Laboratories of Physics Applied to Health and Radiochemistry at LASA: Research Activity

RADIOCHEMICAL/ NUCLEAR METHODS → **Radionuclides** | **Activation analysis** | **Radioactive counting techniques**

Research area	Innovative Radionuclides for medical, toxicological and nanotoxicological use	Engineered nanoparticles (NPs)	Environmental radioactivity / Radioprotection
Project	High Specific Activity RadioNuclides HSARN project	NAnoSafety Research NASAR project	RADioactivity Environ. Measurements RADEM project
Experimental activity	Irradiations, Excitation functions, radioch. sep.	Radiolabelling/ NAA of NPs	Alpha, beta, gamma spectrometry
Studies carried out (examples)	> 70; in the last 6 years ^{99m}Tc, ^{103}Pd; ^{89}Zr; ^{52g}Mn; ^{149,152,155,161}Tb	^{51}TiO2 (Cosmetics) ^{110m}Ag (Food packaging) ^{59}Fe (Uptake by plants)	Measurements after NPP accidents; Measurements of ^{222}Rn indoor
Objectives	Optimisation of radionuclide production (theranostic medicine)	Nanocharacterization, mechanisms of nanotoxicity, nanomedicine, support to industry	Radioprotection Education Dissemination

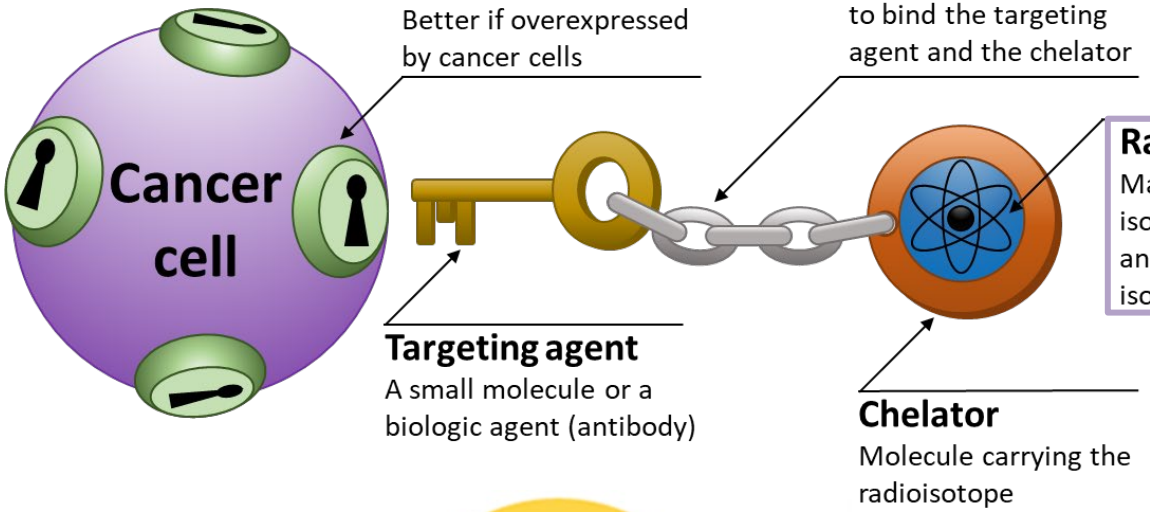
Grazie Renato e Mauro !!!!

Dal 1954 alla fine degli anni sessanta, I.R. Bellobono spostò progressivamente la sua attività scientifica dal campo della dinamica chimica ed elettrochimica a quello della radiochimica e della chimica delle radiazioni, mantenendo sempre saldi i suoi interessi verso le problematiche ambientali, presso il Dipartimento di Chimica di UNIMI

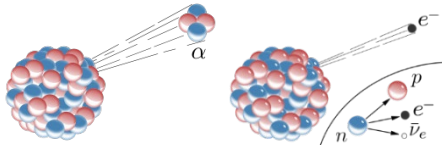
Insieme hanno sempre condiviso il **Corso di Chimica** per il **Corso di Laurea in Fisica** di UNIMI

A partire dal 1978 con l'installazione del primo Laboratorio di Radiochimica presso il Laboratorio Ciclotrone dell'Universita' degli Studi di Milano e successivamente a partire dagli anni '80 con la realizzazione dei Laboratori presso il LASA, ha svolto la sua attività scientifica e di ricerca presso il Dipartimento di Fisica di UNIMI nell'ambito della radiochimica con progetti incentrati sull'impiego dei radionuclidi prodotti mediante ciclotrone per applicazioni mediche ed ambientali.

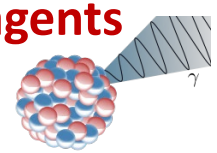
Radionuclides & Radiopharmaceuticals

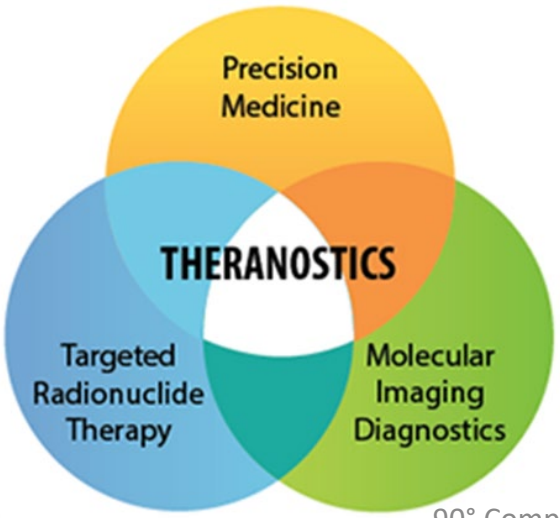


Therapeutic agents



Diagnostic agents





Radionuclides properties:

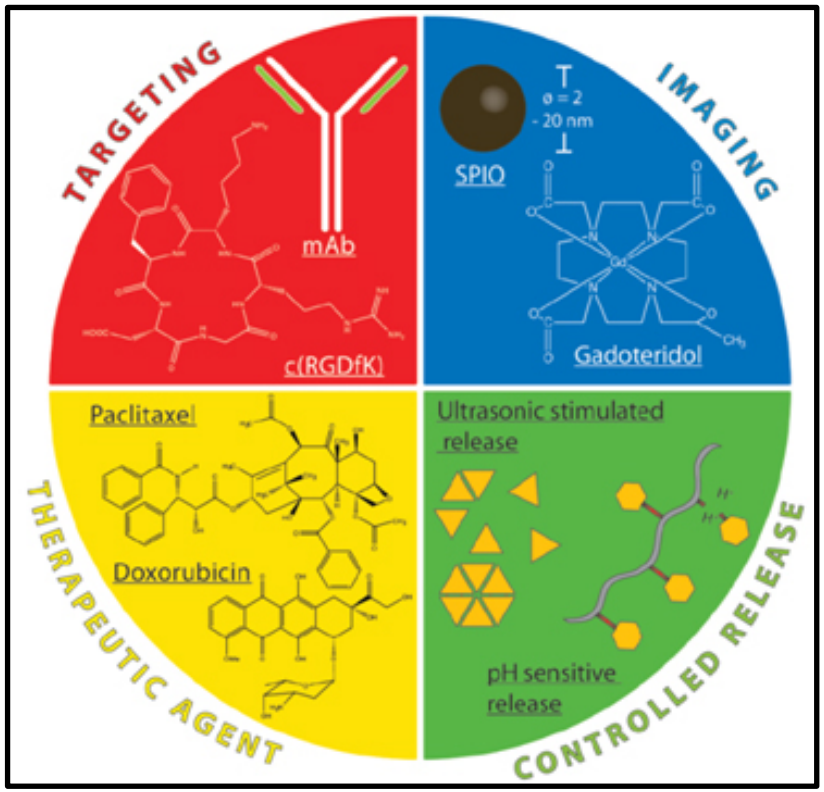
- Decay properties
- Half-life
- Chemical properties
- Production Feasibility

THERANOSTIC MEDICINE

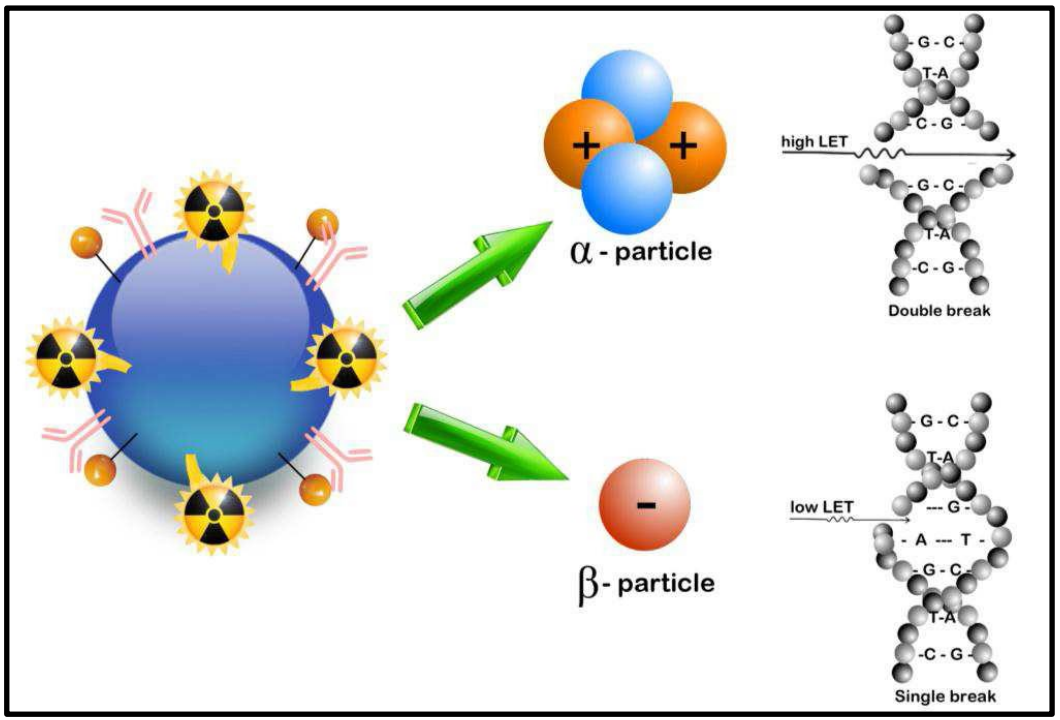
- Theranostic medicine is a new integrated therapeutic system which can **diagnose**, **deliver targeted therapy** and **monitor the response to therapy**.
- the nuclear physician can **follow the real biodistribution of the radiopharmaceutical inside** the patient after the injection and the **follow-up during the repeated treatments**.
- The radioisotopes used for **metabolic radiotherapy are α, β and Auger electron emitters**. Many of them are also **γ** emitters and can be **detected by gamma-camera, SPECT or PET**.
- Many of these "neutron reach" radionuclides are produced by nuclear reactor with a very low A_S. In selected cases they can be produced by bombardment of targets by charged particle beams, in No Carrier Added Form – NCA - with very high A_S

Nanoparticles and theranostic nanomedicine

Multifunctional design of a micelle nanomedicine platform with cancer targeting, imaging, controlled release properties.



Blanco et al.,
Exp.Biol. Med.2009, 234:123-131

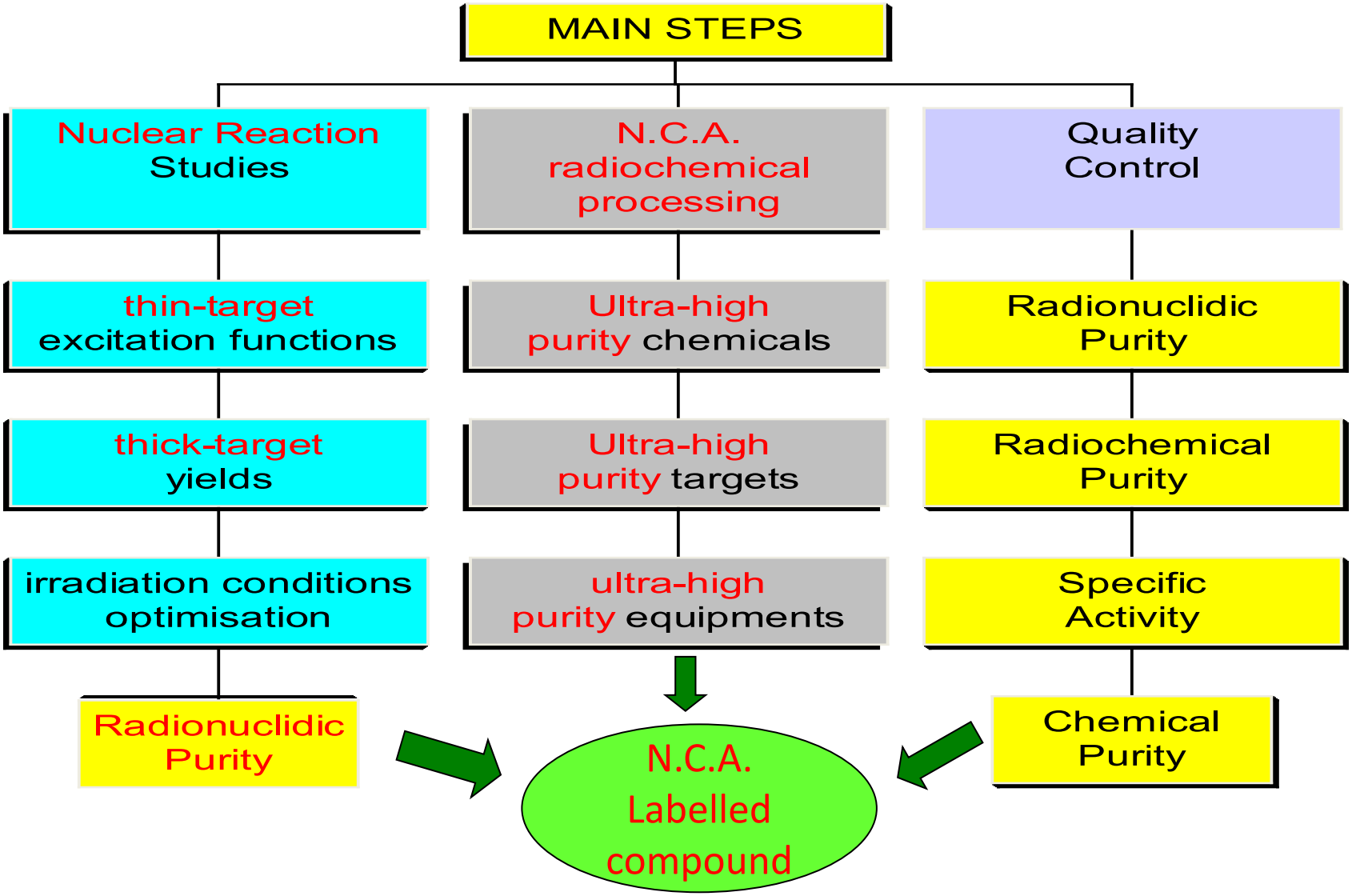


E. Morales-Avila et al. Radiolabeled Nanoparticles for Molecular Imaging (2012) in Molecular Imaging Ed. by B.Schaller, InTech

Radionuclides for metabolic radiotherapy and theranostics

radionuclide	Half-life days	β-max MeV	R soft tissue mm	Eγ keV
Dy-165	0.1	1.29 (83%); 1.19 (15%)	5.7	95 (4%)
Sm-156	0.4	0.7 (51%); 0.4 (44%)		none
Re-188	**0.7**	**2.12 (72%); 1.96 (25%)**	**11.0**	**155 (15%)**
Ho-166	**1.2**	**1.85 (51%); 1.77 (48%)**	**8.5**	**81 (6%)**
Rh-105	1.5	0.57 (75%); 0.25 (20%)		319 (19%)
Sm-153	**1.9**	**0.67 (78%); 0.81 (21%)**	**2.5**	**103 (28%)**
Au-198	2.7	0.96 (99%)	3.6	411 (96%)
Y-90	**2.7**	**2.28 (100%)**	**11**	**none**
Re-186g	**3.7**	**1.07 (74%); 0.93 (21%)**	**3.6**	**137 (10%)**
Yb-175	4.2	0.47 (87%)		396 (7%)
Lu-177g	**4.2**	**0.48 (78%)**	**1.7**	**208 (11%)**

Production, Radiochemical Processing and QC/QA of *No Carrier Added* (n.c.a.) labelled species



Theoretical SA(CF) :

$SA(CF) = N_A \lambda / P_a \qquad [Bq\ g^{-1}]$

Specific Activity, SA :

SA = Activity of a RN / mass isotopic carrier

Isotopic Carrier :

total number of atoms “isotopic”
with main Radio-Nuclide
(both radioactive and stable)

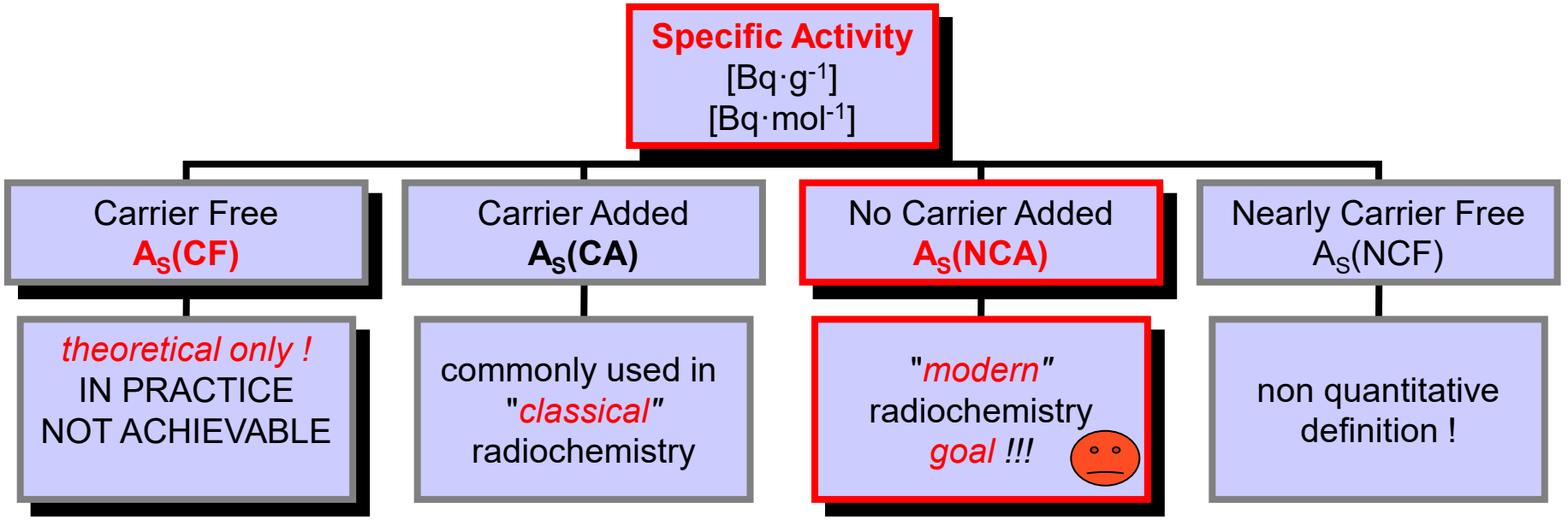
Isotopic Dilution Factor :

IDF = total number of isotopic atoms
divided
number of atoms of RN

Kinds of A_S

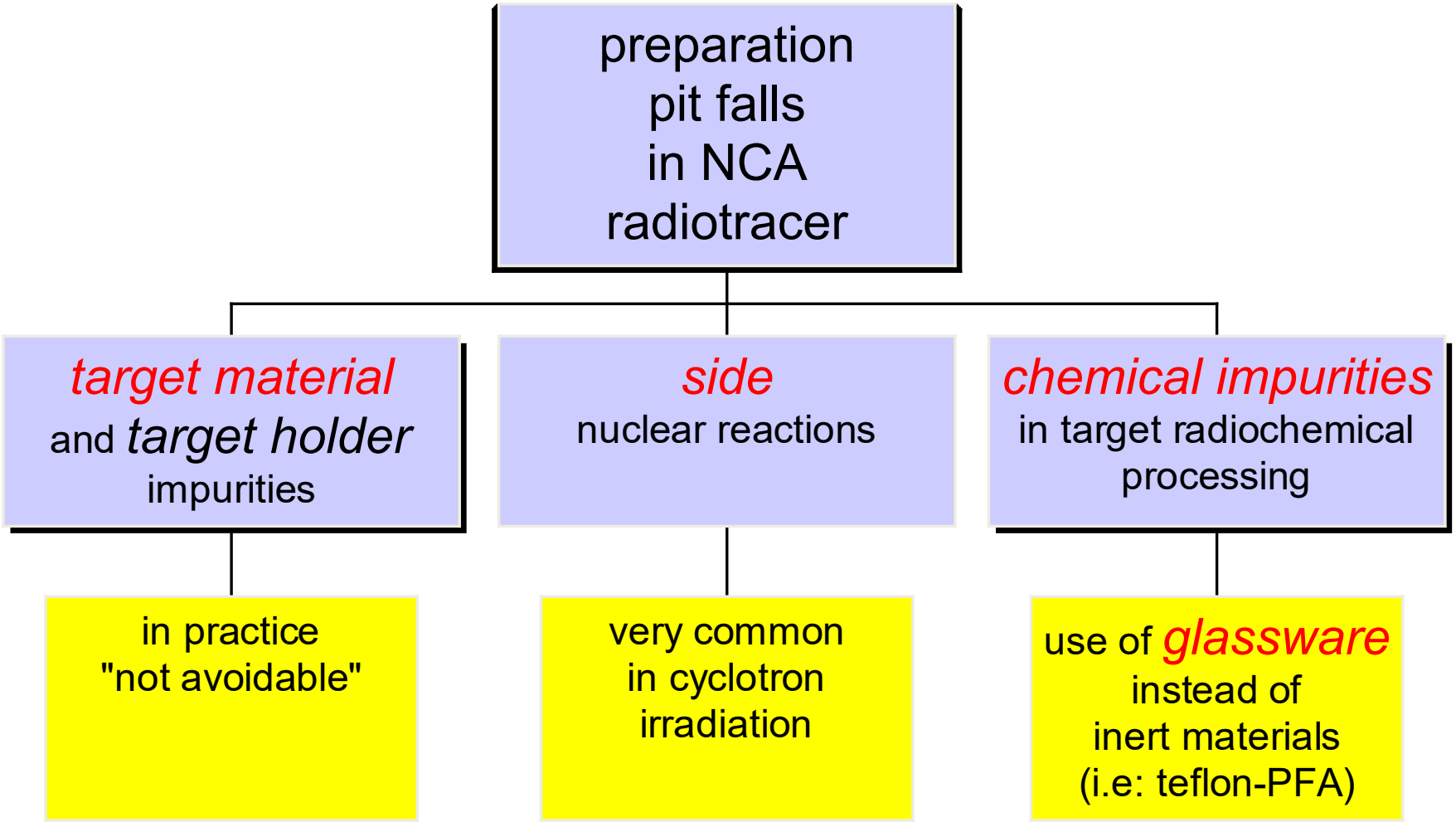
Alfred P. Wolf, Brookhaven National Laboratory, USA

J. Nucl. Med. 22 (1981) 392-393



A_S must not be confused with
Radioactivity Concentration [Bq·g^{-1}]:
(same units but the meaning is completely different)

Origins of Isotopic Carrier (both stable and radioactive)



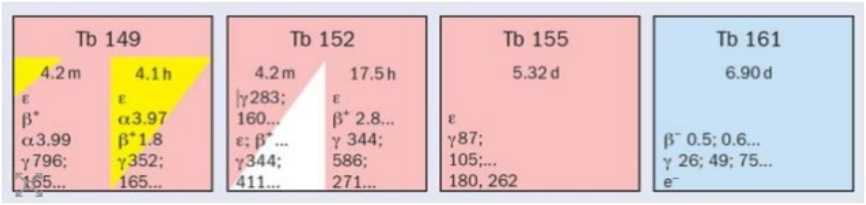
Advantages if the irradiations are made with deuteron beams

- the **higher stopping power** in respect to the protons allows to employ targets with smaller thickness: the volume of reagents, the synthesis systems and the discharge of radioactive material for radioprotection purpose are smaller, the **A_S and chemical purity** of the final product **are higher**.
- deuterons usually present higher cross sections in compound nucleus region.

NEWS

Terbium: a new 'Swiss army knife' for nuclear medicine

28 January 2013



Terbium which comprises four medically interesting radioisotopes: the "Swiss army knife" for diverse applications in nuclear medicine.

WHY terbium isotopes

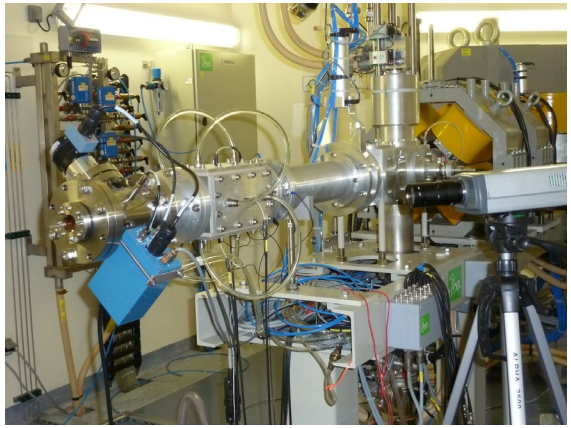
Imaging

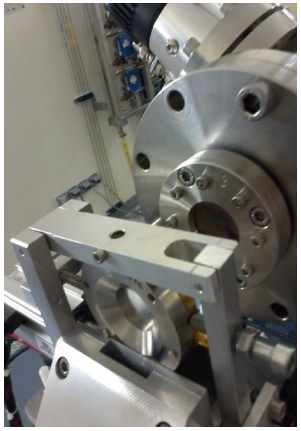
Therapy

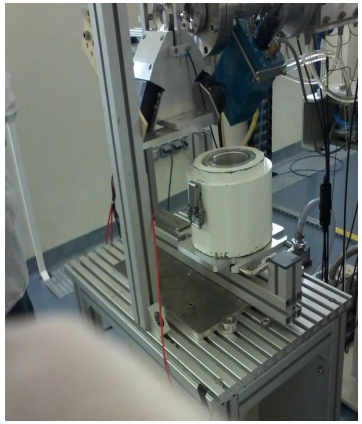
Isotope	$T_{1/2}$	β^+ E_{aver} [keV] (I)	X and γ with I > 10% [keV] (I)	β- E_{aver} [keV] (I)	Conv. & Auger (>1 keV) E_{aver} [keV] (I)	α En. [keV] (I)
^{149}Tb	4.1 h	730 (7%)	42-50 (69%), 165 (26%), 352 (29%), etc.	-	32 (85%)	3967 (17%)
^{152}Tb	17.5 h	1140 (20%)	42-50 (65%), 344 (64%)	-	36 (69%)	-
^{155}Tb	5.32 d	-	42-50 (108%), 87 (32%), 105 (25%)	-	19 (204%)	-
^{161}Tb	6.89 d	-	45-53 (39%), 75 (10%)	154 (100%)	19 (227%)	-

ACCELERATOR → ARRONAX Cyclotron (Nantes)

Protons	35 - 70 Mev	up to 750 μA
Deuterons	15 – 35 Mev	
Alpha	70 MeV	



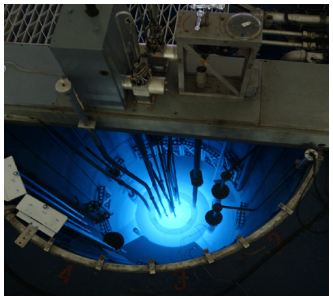




LASA

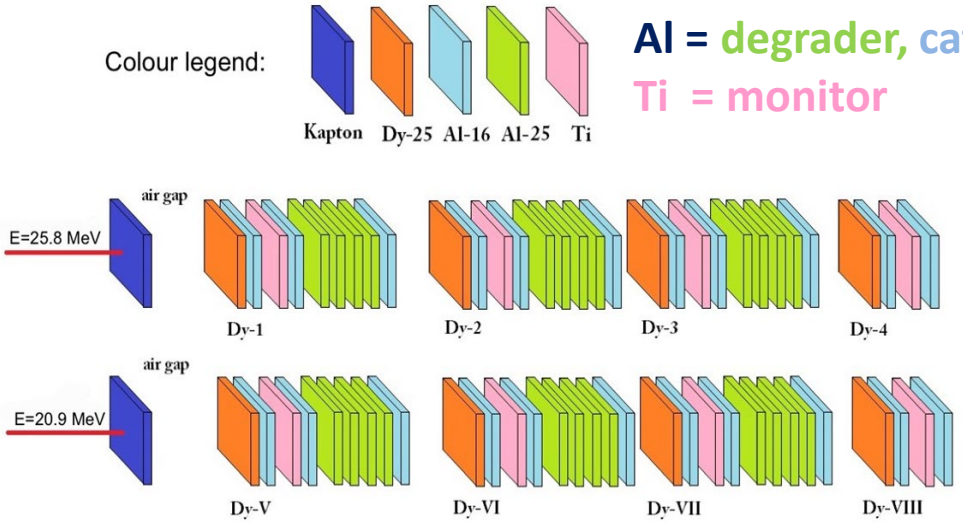
- Radiochemistry Laboratory
  Low and medium activities of γ,β,α radionuclides are radiochemically processed
- Physics and Chemistry
- Measurements Laboratory

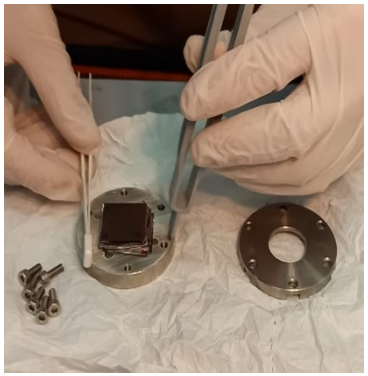
LENA - Pavia →

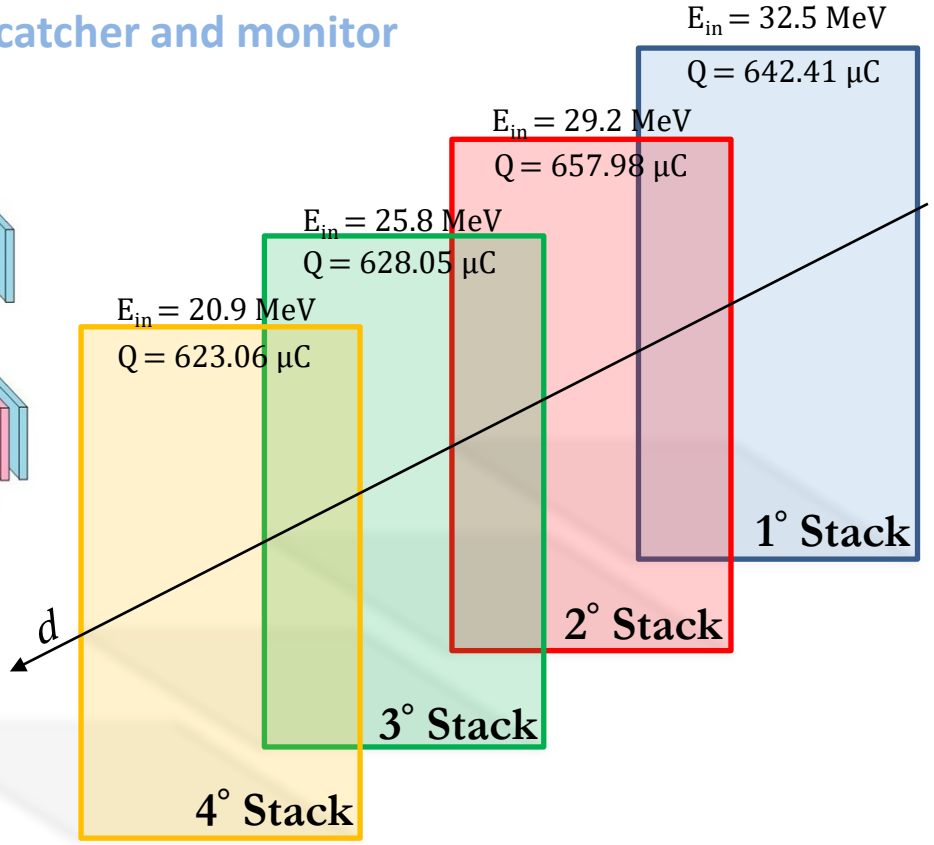


Nuclear Reactor TRIGA MARK II

Irradiation of thin ^{nat}Dy targets with the stacked foils technique





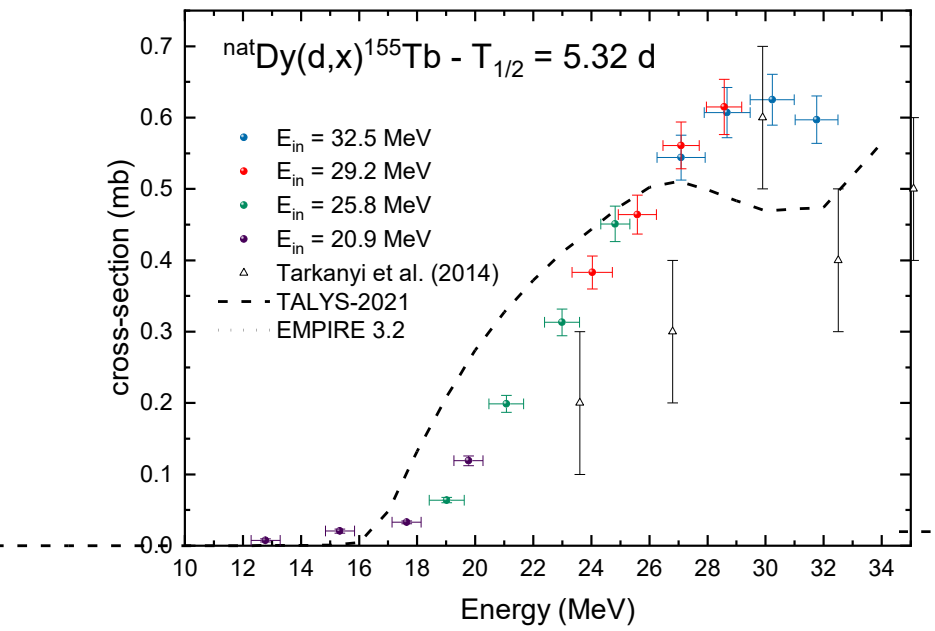


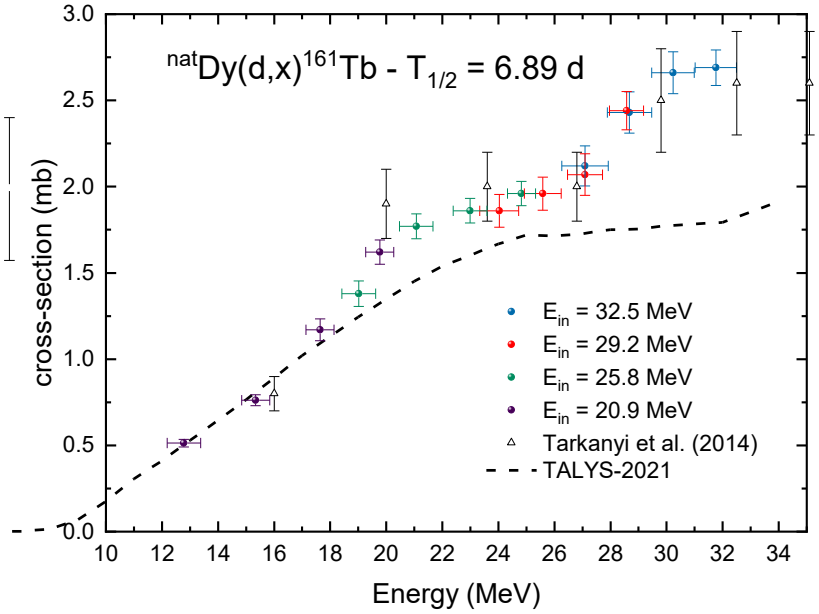
2 irradiations at ARRONAX, Nantes, 2 stacks each time

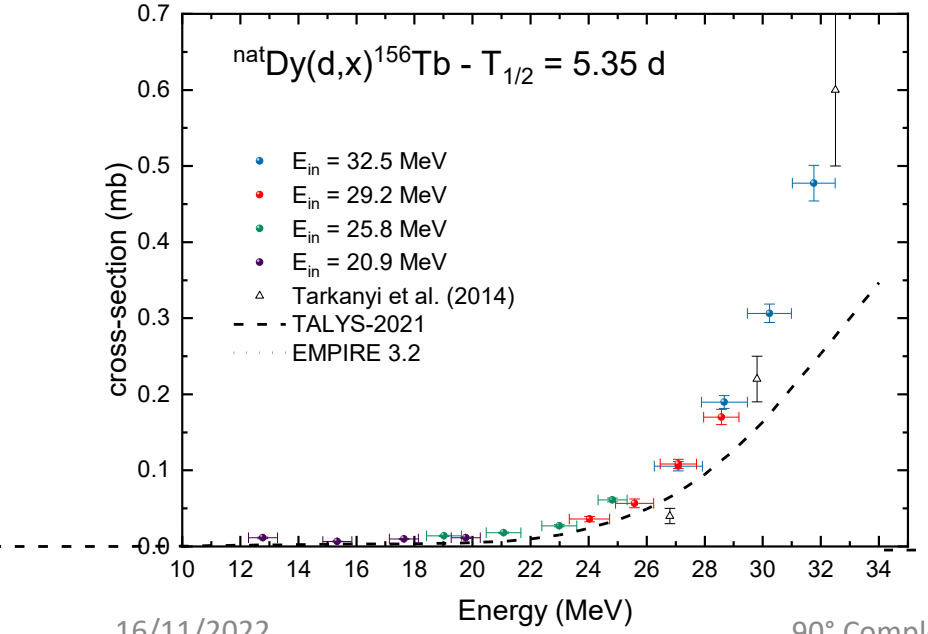
- **Thin natural ^{nat}Dy targets: nominal thickness of about 25 µm and a general relative uncertainty of ±2%**
- **Irradiation time: 60 min**
- **Beam current: 150 nA**

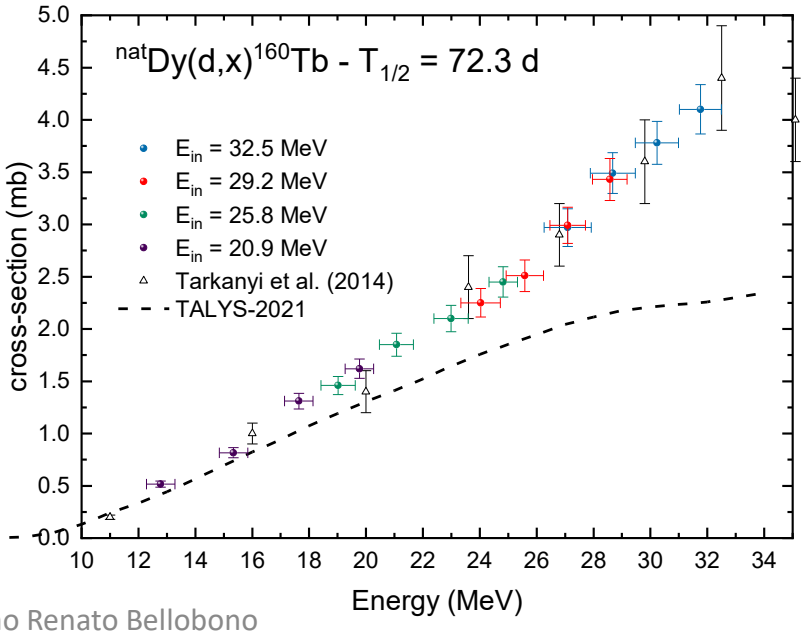
^{nat}Dy targets: ^{156}Dy 0.06%; ^{158}Dy 0.10%; ^{160}Dy 2.24%; ^{161}Dy 18.9%; ^{162}Dy 25.5%; ^{163}Dy 24.9%; ^{164}Dy 28.2%

Excitation functions of $^{nat}Dy(d,x)^{1XX}Tb$



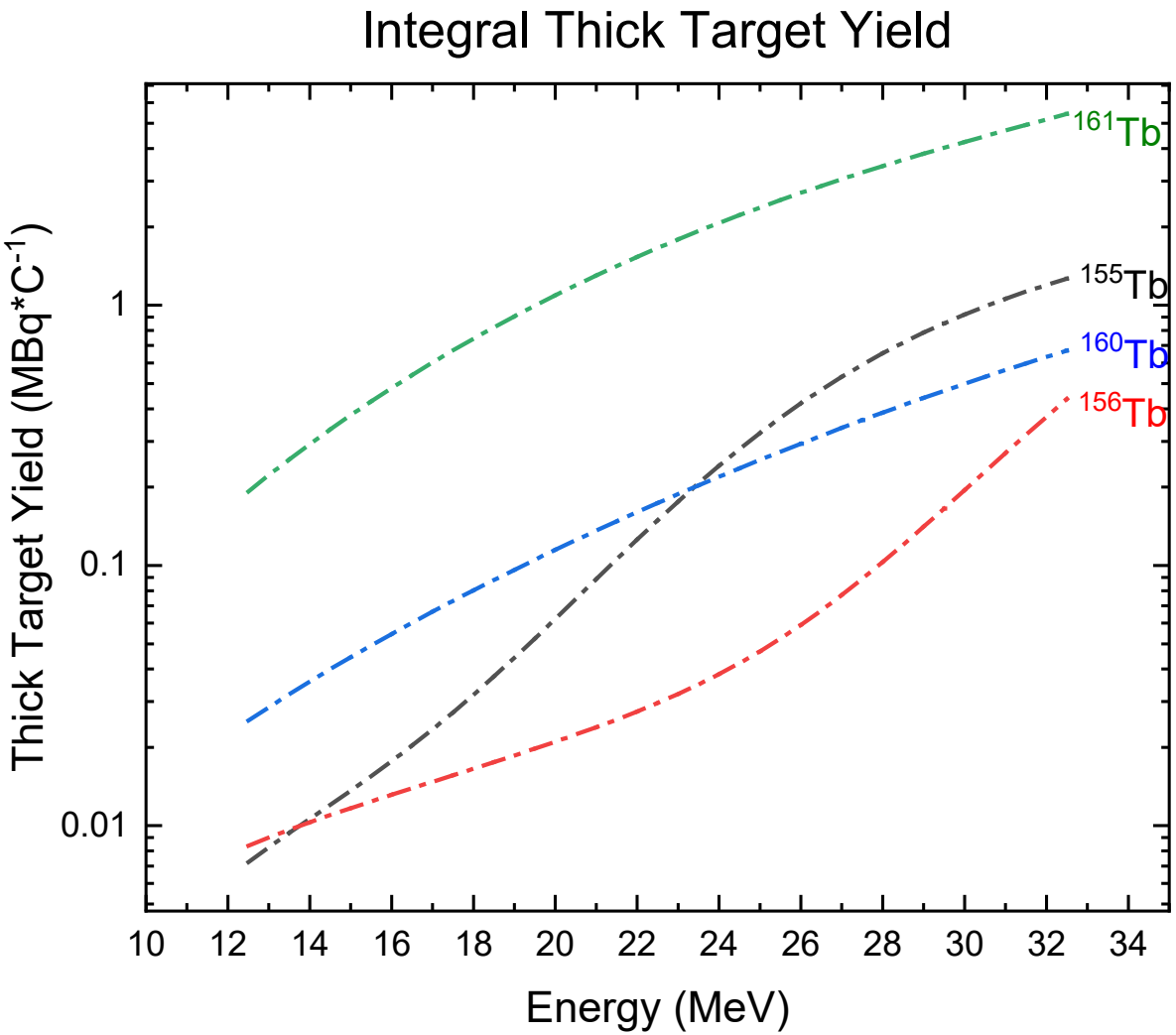






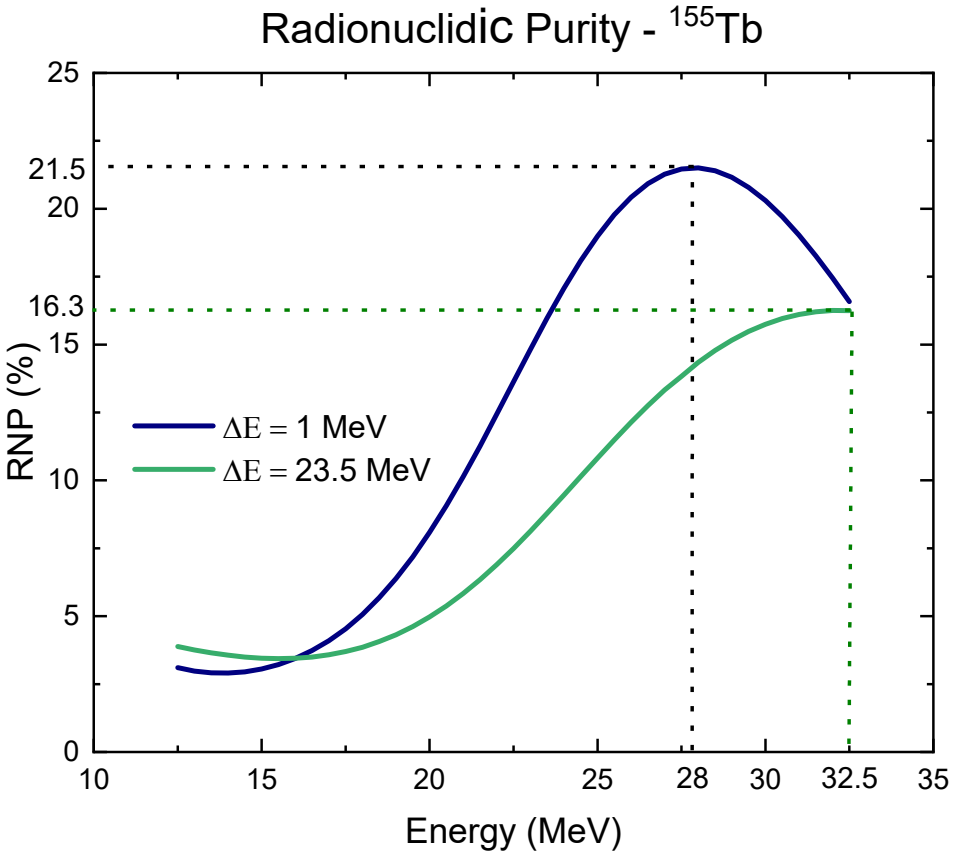
Thick Target Yield of $^{nat}Dy(d,x)^{1xx}Tb$

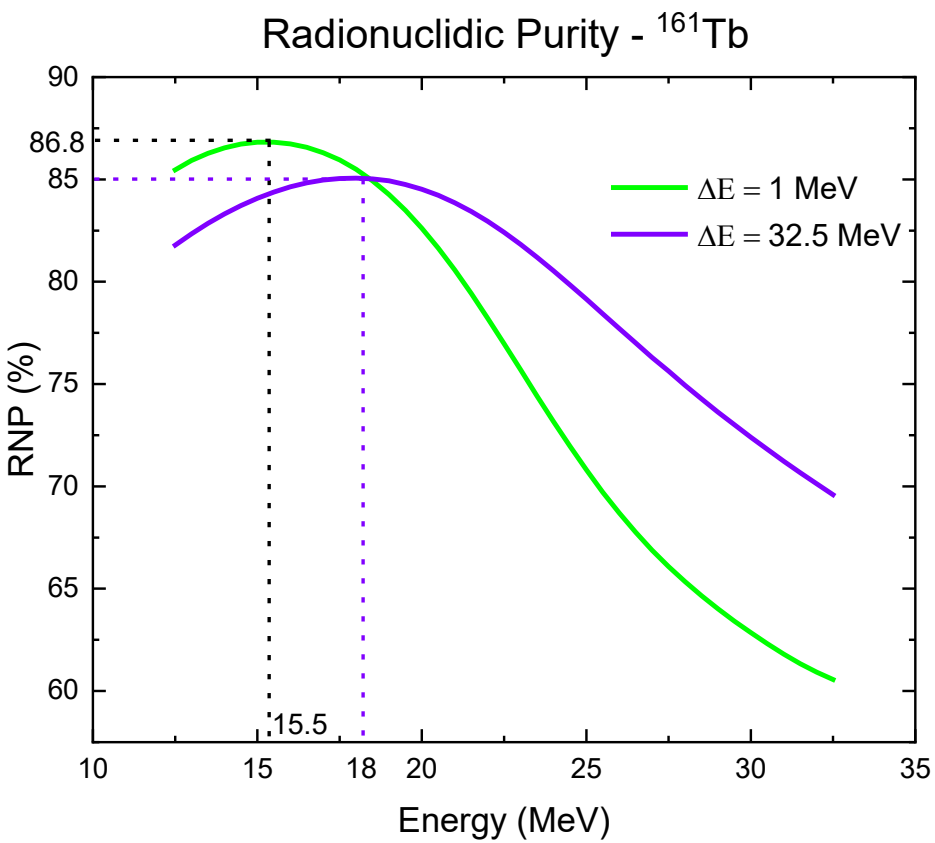
$$y(E)_{EOIB} = \frac{\sigma(E) \cdot N_A \cdot \lambda}{M \cdot Ze \cdot \frac{1}{\rho} \cdot \frac{dE}{dx}(E)} \quad \left[\frac{Bq}{C \cdot MeV}\right] \qquad Y(E, \Delta E) = \int_{E-\Delta E}^{E} y(E)\, dE \quad \left[\frac{Bq}{C}\right]$$



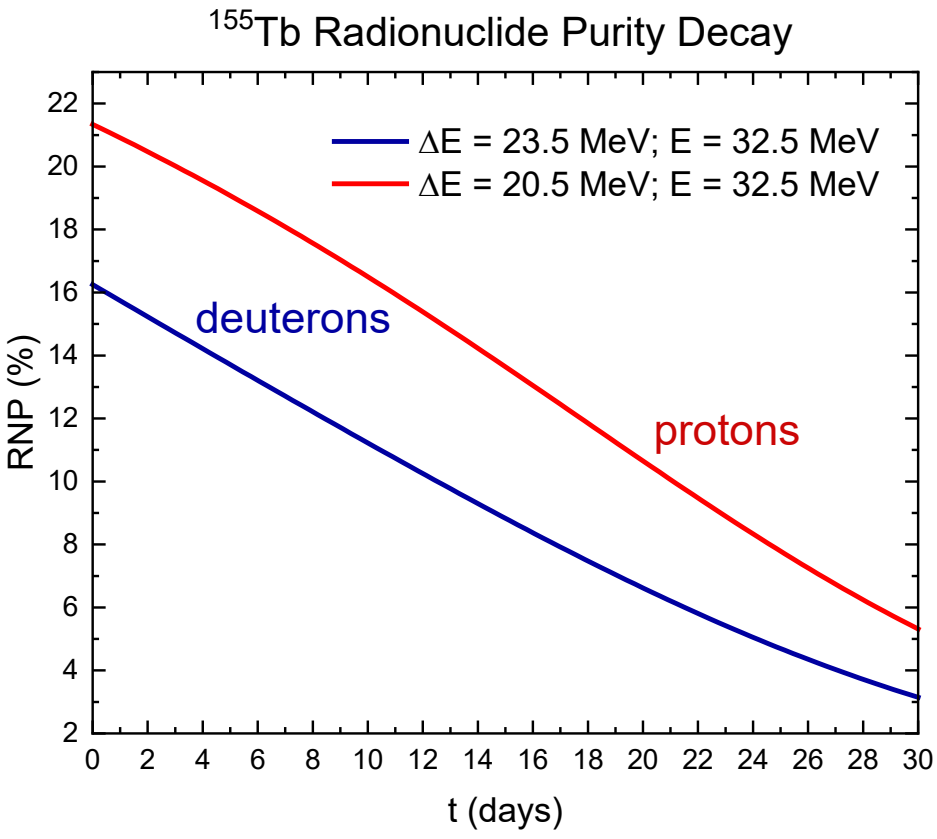
Radionuclidic Purity of $^{nat}Dy(d,x)^{1xx}Tb$

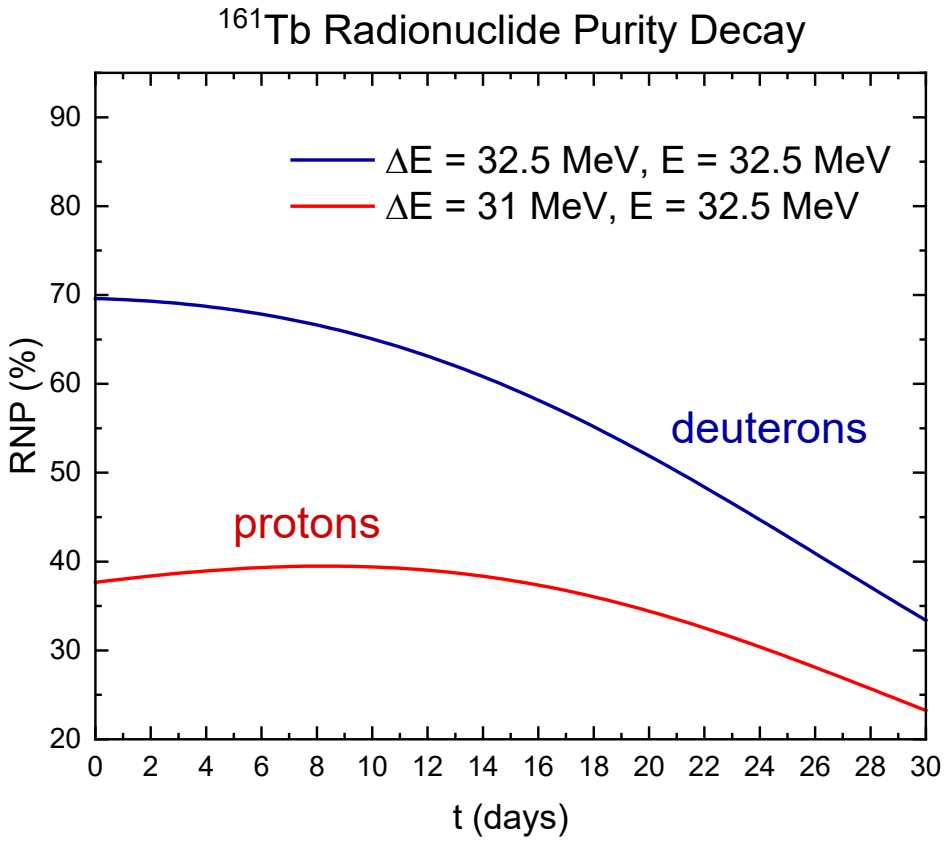
$$RNP_{\%}(t) = \frac{A_i\,(t)}{\sum_j A_j(t)} \cdot 100 = \frac{A\left({}^{155/161}_{65}Tb\right)}{A\left({}^{155}_{65}Tb\right)+A\left({}^{156}_{65}Tb\right)+A\left({}^{160}_{65}Tb\right)+A\left({}^{161}_{65}Tb\right)}$$



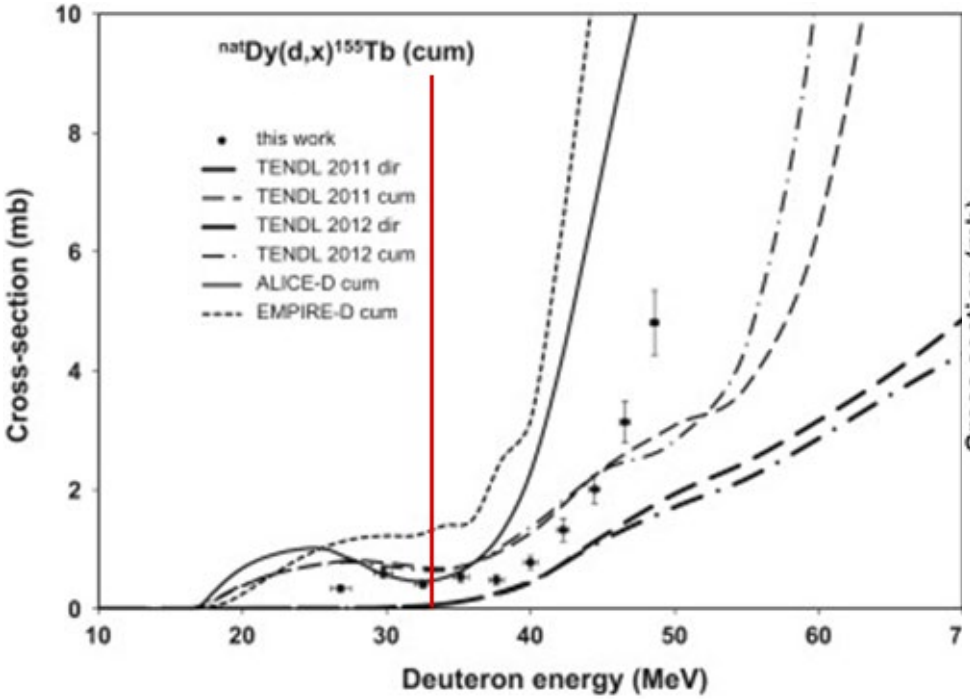


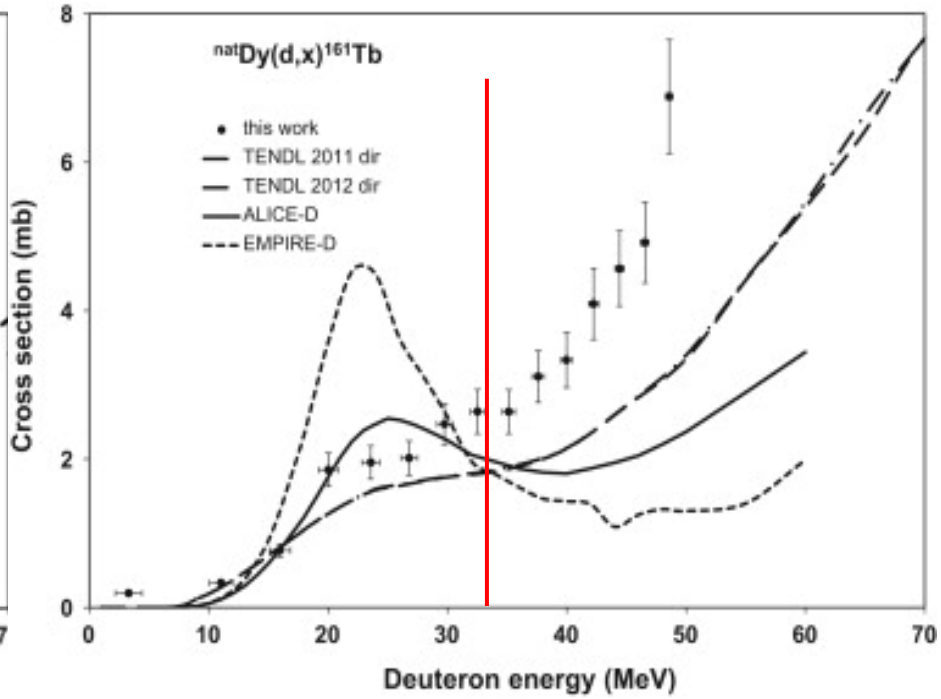
Radionuclidic Purity of $^{nat}Dy(d,x)^{1xx}Tb$





CONCLUSIONS





Or for ^{155}Tb other production routes:
The indirect production via the decay of ^{155}Dy
BUT
The unavoidable presence of ^{157}Dy with a TTY higher than ^{155}Dy

The use of high enriched target in ^{156}Dy with the study of what energy window could allow to reduce the presence of ^{157}Dy and obtain a ^{155}Dy-^{155}Tb generator with very high specific activity.

CONCLUSIONS

- There are different possibility to produce and to have theranostic radionuclides;
- The deuteron induced nuclear reactions can be a real challenger to obtain radionuclides with very high specific activity
- The problem is that the number of cyclotrons that can deliver deuterons with the suitable energies and beam current is very low.

Grazie per la vostra attenzione

e

AUGURI di BUON COMPLEANNO