NON CONVENTIONAL PRODUCTION OF RADIONUCLIDES BY PARTICLES ACCELERATORS FOR BIOMEDICAL APPLICATIONS

F. Groppi, M.L. Bonardi, S. Manenti, E. Sabbioni

Radiochemistry Laboratory, LASA,

Universita' degli Studi di Milano and

INFN Sez. Milano and Legnaro

e-mail: flavia.groppi@mi.infn.it

Relevant applications of radiotracers and labelled compounds in No Carrier Added form

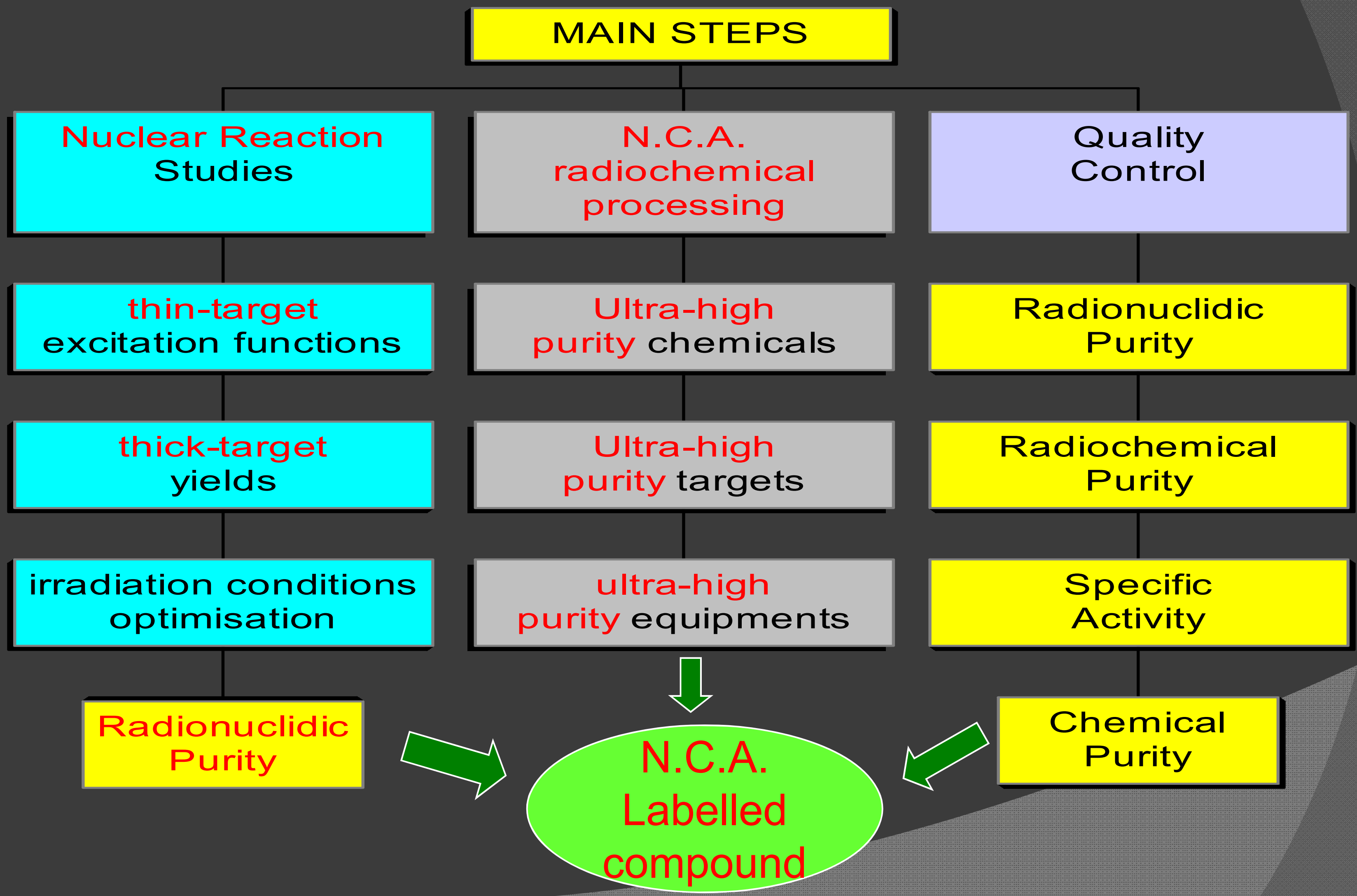
some relevant applications

1. metallo-biochemistry 2. cellular biology	environmental toxicology at low doses	1. nuclear medicine 2. metabolic radiotherapy
behaviour of **different chemical forms** of **trace elements**	**Low Level** and **Long Term Exposure** (LLE) to **ultra-trace elements**	radiodiagnostics (SPECT, PET) systemic radionuclide tumour radiotherapy
speciation studies **synergistic effects**	**speciation studies** **dose-effect relationships**	radioimmunotherapy of tumours

THERAGNOSTIC MEDICINE

- Theranostic medicine is a new integrated therapheutic 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 specific activity - 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

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



Moreover the experimental determination of:

- ✓ **Biological Purity (for applications in the life sciences, biological and human)**
- ✓ **Stability vs. Time of all previous parameters, both *in-vitro* and *in-vivo***

Specific Activity determination techniques

Any "**elemental analysis**" technique combined with any kind of "**radiometric technique**"

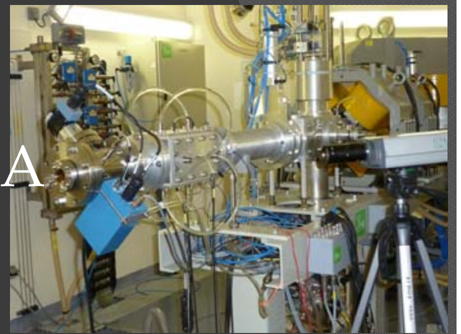
- **Atomic absorption** (GF-AAS), **atomic emission** spectrometries (ICP, ICP-MS)
- **Elettroanalytical** (ASV, CSV)
- **Mass spectrometric** (many kinds)
- **Neutron** and **charged particle activation analysis**, both instrumental and radiochemical
- **Radio-release** techniques
- **High-resolution X, γ, β, α spectrometries**
- **Liquid Scintillation Counting** (LSC)

Hyphenated techniques $\rightarrow$ ***Goal***

Involved laboratories

The research activity of the Milano Group is carried out at the following laboratories:

ARRONAX Cyclotron (Nantes)



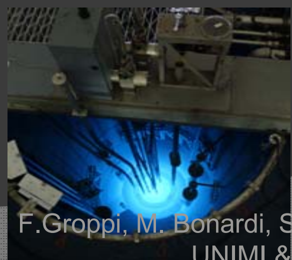
Beam particles

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

LASA → Radiochemistry Laboratory

LASA → Physics and Chemistry Measurements Laboratory

LENA - Pavia → Nuclear Reactor TRIGA MARK II



Radionuclides for metabolic radiotherapy and theragnostics

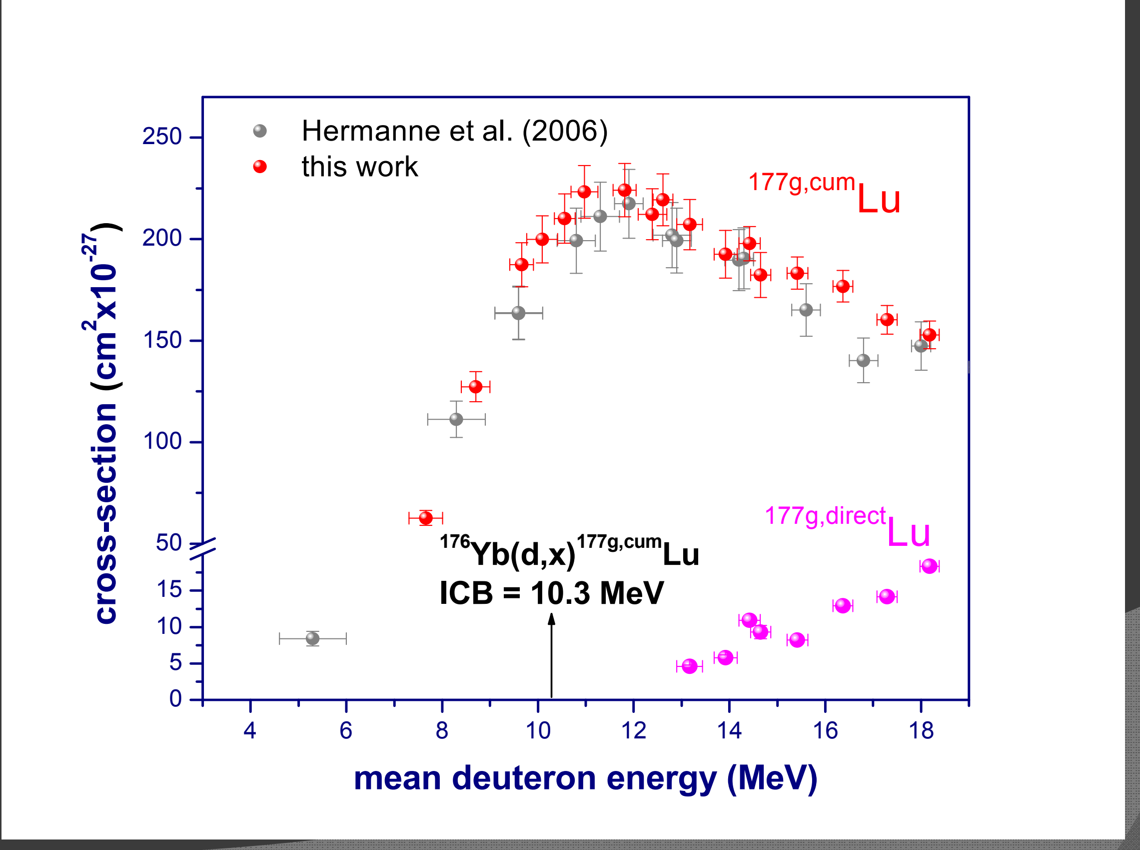
radionuclide	Half-life days	β-max MeV	R soft tissue mm	Eγ keV
Dy-165	0.1	1.29 (83%); 1.19 (15%)	5.7	95 (4%)
Sm-156	0.4	0.7 (51%); 0.4 (44%)		none
Re-188	**0.7**	**2.12 (72%); 1.96 (25%)**	**11.0**	**155 (15%)**
Ho-166	**1.2**	**1.85 (51%); 1.77 (48%)**	**8.5**	**81 (6%)**
Rh-105	1.5	0.57 (75%); 0.25 (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%)**

Some examples: more recently studies

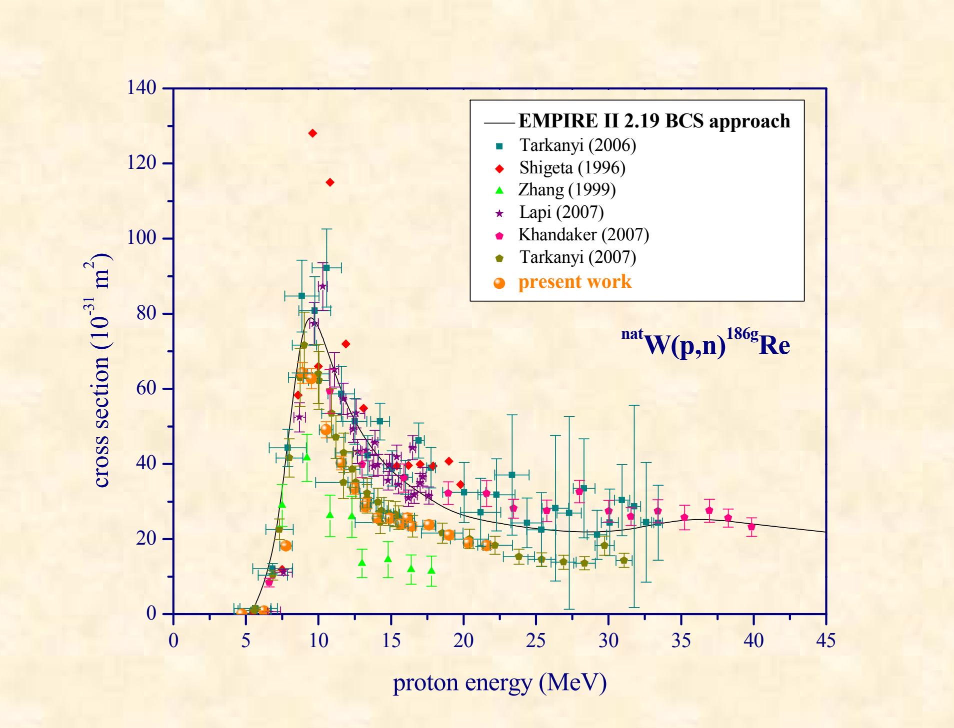
Measured cross sections in the range up to 19 MeV and set up of radiochemical separations for:

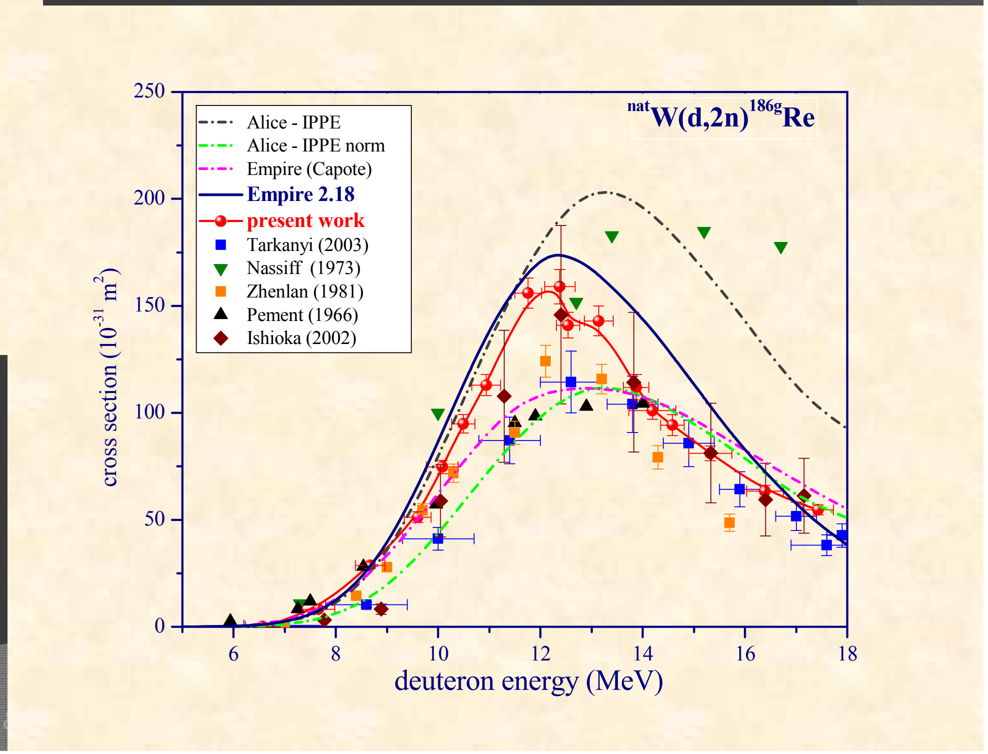
$^{186}W(d,2n)^{186g}Re$, $^{176}Yb(d,p)^{177g}Lu$

to be used in metabolic radiotherapy and for paliative treatment of bone metastasis pain.

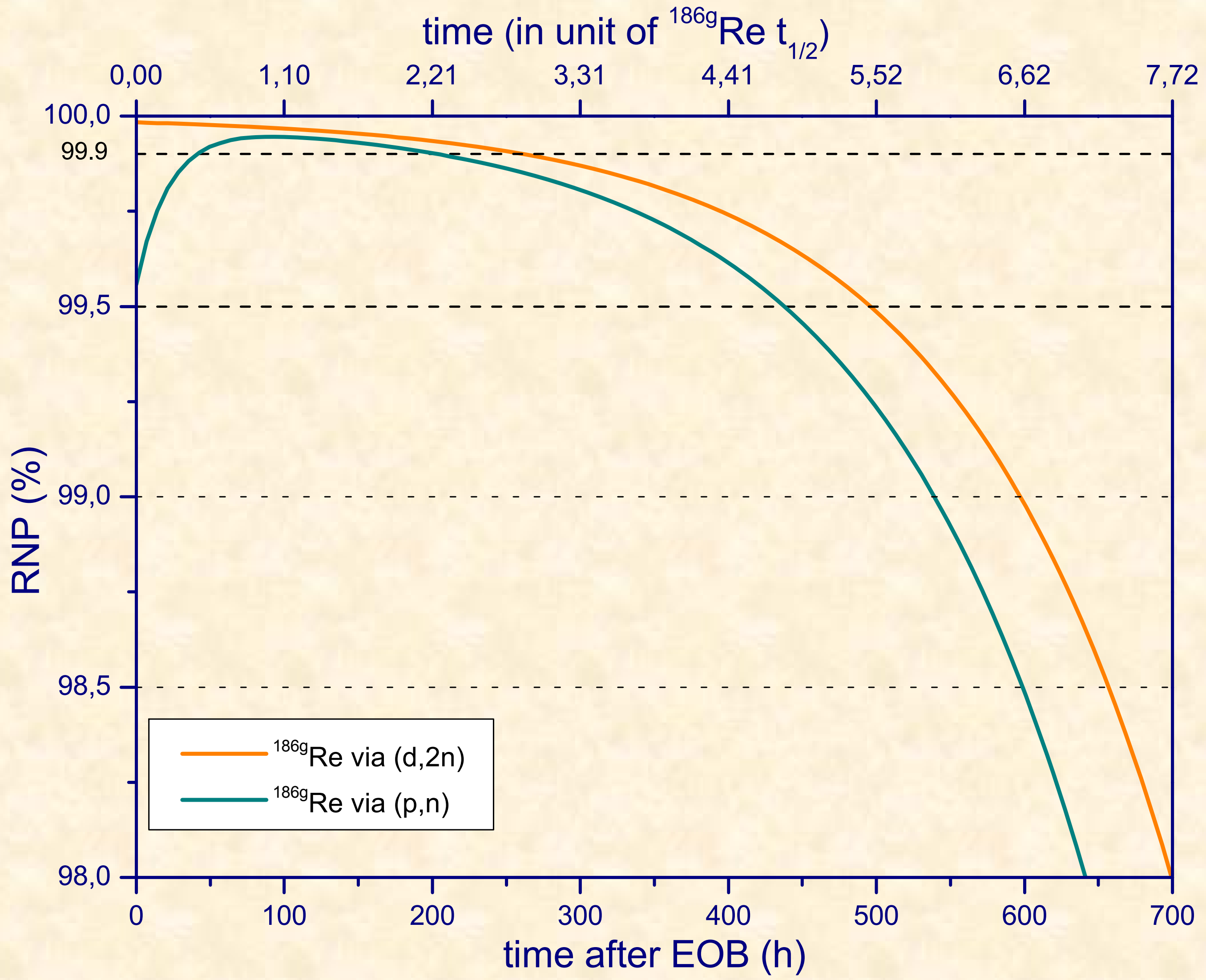


Comparison between cross sections for W(p,n)^{186g}Re and W(d,2n)^{186g}Re





Comparison of radionuclidic purity for different ^{186g}Re production methods on ^{186}W enriched target

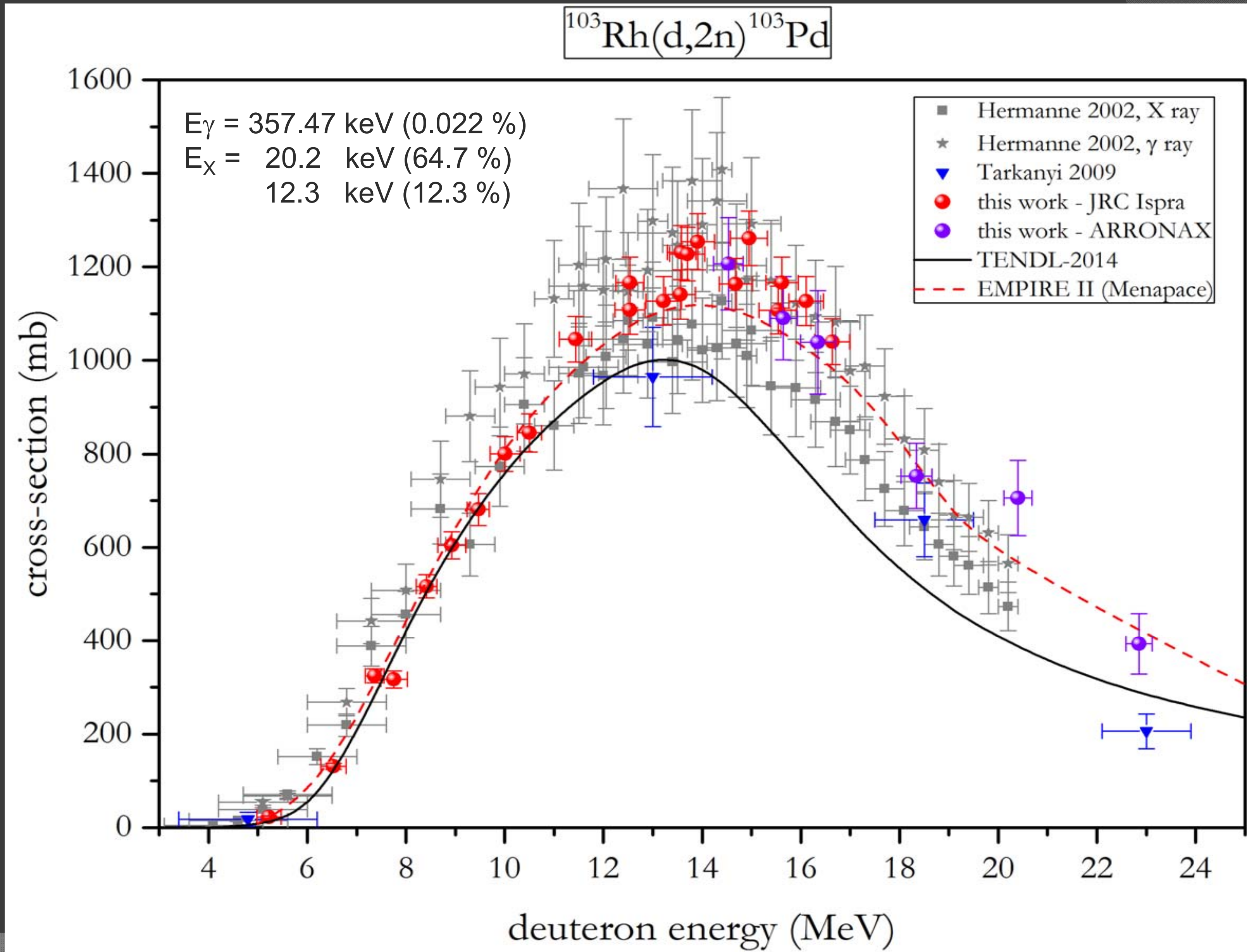


Future Programme
collaboration with ARRONAX, France

Often the (n,γ) reactions lead to non-sufficiently high specific activity (in CA form), thus alternative NCA methods are required.
Hot-atom recoil method (i.e. Szilard-Chalmers) is inefficient.

- ^{103}Rh (d,2n) ^{103}Pd NCA
  prostate brachytherapy (SS or Ti seeds)
- ^{89}Y (d,2n) ^{89}Zr NCA
  for PET and immuno-radiotherapy
- ^{110}Pd (d,2n) ^{111}Ag NCA
  silver nanospheres and metal chelates
- ^{198}Pt (d,2n) ^{199}Au NCA
  gold nanospheres and metal chelates

Cross Section of $^{103}Rh(d,2n)^{103}Pd$ ($t_{1/2}$ = 16.96 d)

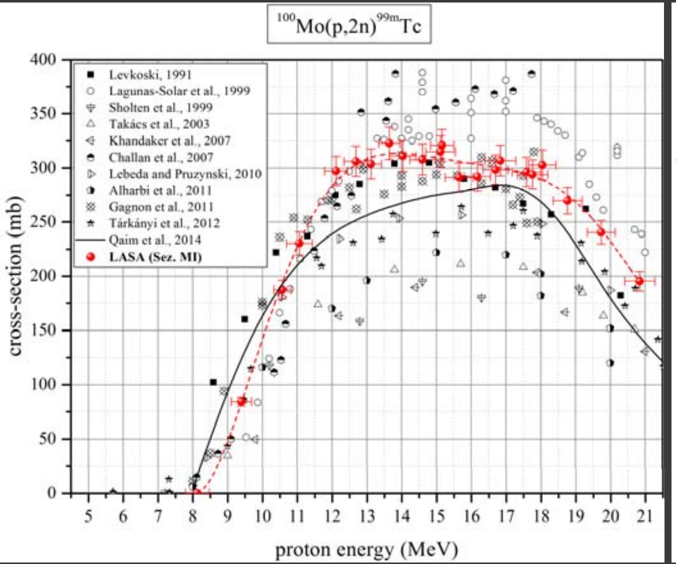


For the future utilization of the new cyclotron at LNL

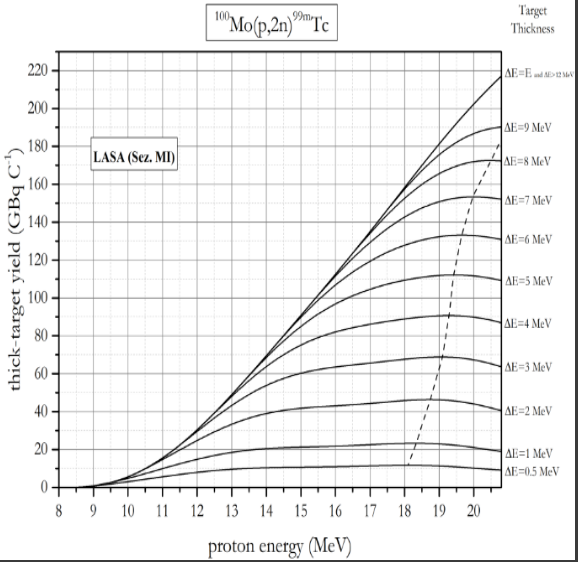
a) Experimental measurements of the cross sections for the different reaction channels for the ^{100}Mo(p,xn) nuclear reaction; determination of the Thick Target Yields to define the optimal irradiation conditions

b) In collaboration with INFN-PV set up of the radiochemical separation of Tc from Mo target and interferences and the recovery of Mo

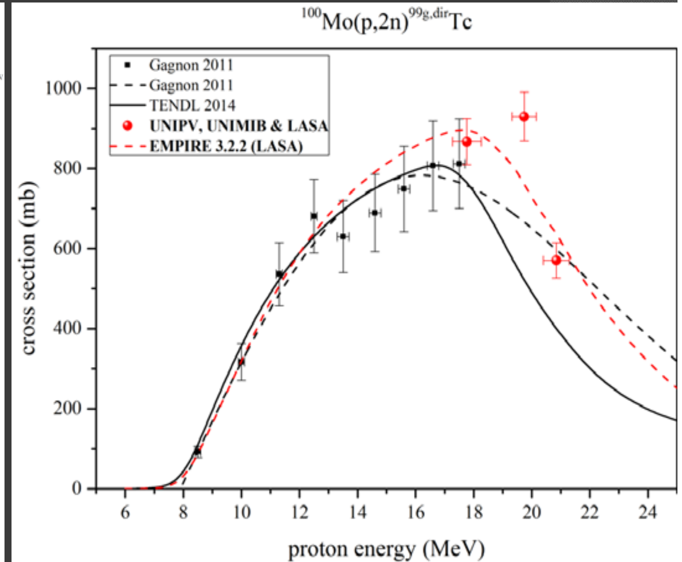
a) Cross Section of ^{100}Mo(p,2n)^{99m}Tc



a) Thick Target Yield of ^{100}Mo(p,2n)^{99m}Tc



b) Cross Section of ^{100}Mo(p,2n)^{99g,dir}Tc



S. MANENTI, U. HOLZWART, M. LORIGGIOLA, L. GINI, J. ESPOSITO, F. GROPPI, F. SIMONELLI, The excitation functions of Mo-100(p,x)Mo-99 and Mo-100(p,2n)Tc-99m, Applied Radiation and Isotopes. 94 (2014) 344

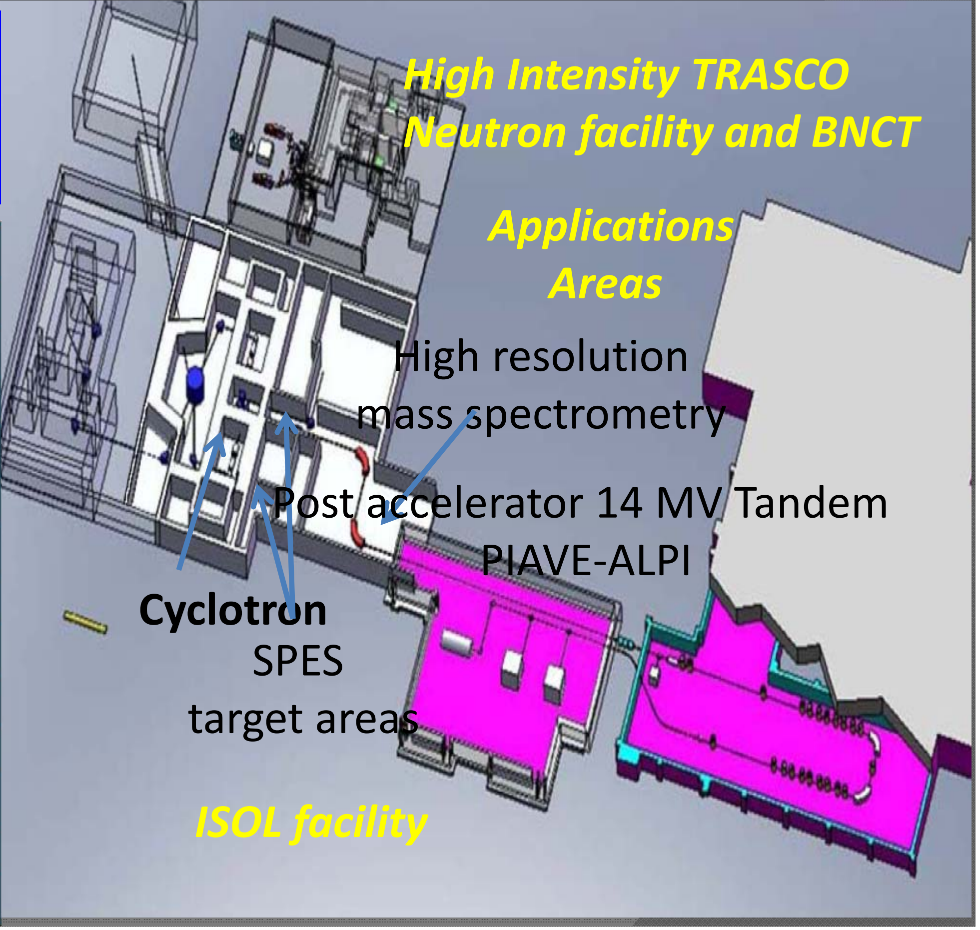
IAEA CRP project F22062 (Dec 2011 – Dec. 2015), INFN Research Activities Progress Report (as of June 2015) on Accelerator-based Alternatives to non-HEU Production of Mo-99/Tc-99m

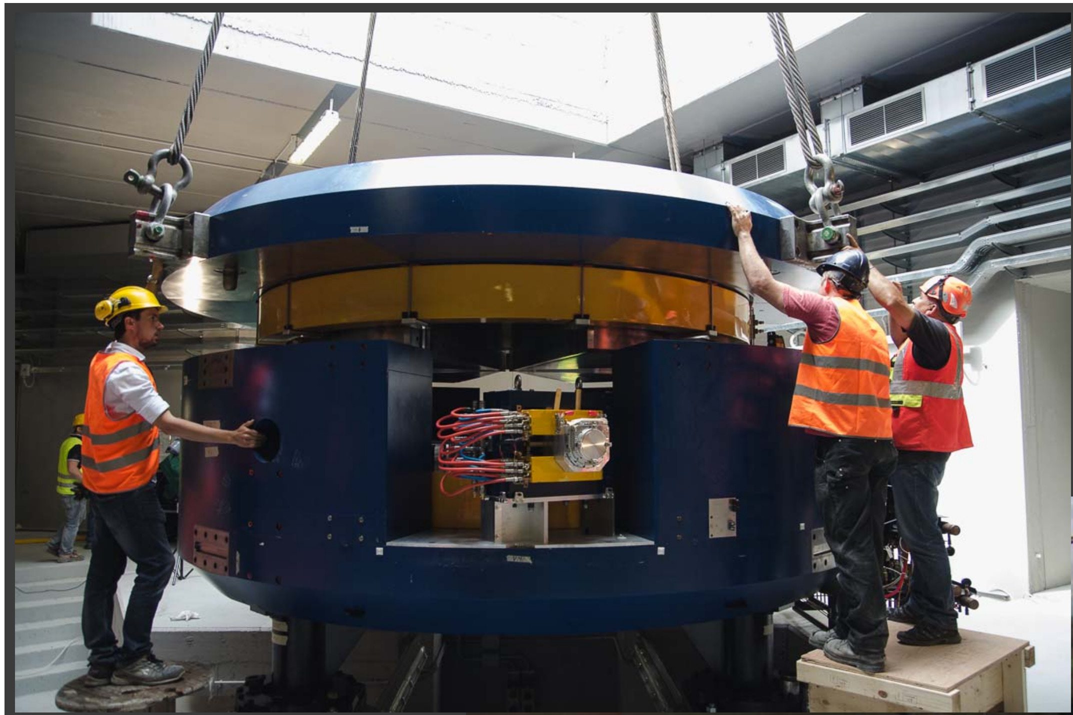
THE FUTURE
A CYCLOTRON ISOTOPE PRODUCTION CENTER FOR BIOMEDICAL RESEARCH
at INFN National Laboratory of Legnaro (PD)

Best Theratronics has been awarded a contract to construct a **70 MeV Cyclotron** for the INFN National Laboratory of Legnaro, Italy

Some proton-cyclotron isotope production
(*enriched target)
Possibility of twin target irradiation

radionuclide	target	reaction	p energy (MeV)	σ_{max} (mbar)
Cu-64	Ni	^{nat}Ni(p,n)	40	50
*Cu-64	Ni	^{64}Ni(p,n)	15	675
Cu-67	ZnO	^{68}Zn(p,2p)	70	25
Ge-68	Ga	^{69}Ga(p,2n)	45	100
*Ge-68	Ga	^{69}Ga(p,2p)	20	550
Sr-82	RbCl	^{nat}Rb(p,4n)	50	100
I-124	Te	^{nat}Te(p,n)	53	150
*I-124	Te	^{124}Te(p,n)	12	590
*Re-186	W	^{186}W(p,n)	10	17
Pd-103	Rh	^{103}Rh(p,n)	10	500
Th-228	Th	^{232}Th(p,X)	70	60
Ac-225	Th	^{232}Th(p,X)	60	3
Pa-230	Th	^{232}Th(p,3n)	30	260






SPES
www.lnl.infn.it
13/11/2014
13:00