

Terzo Incontro Nazionale di Fisica Nucleare, Laboratori Nazionali di Frascati

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Cross section measurements of proton-induced nuclear reactions for
the production of radionuclides for nuclear medicine:

A collaboration between INFN-LNL and ARRONAX facility

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The New 70 MeV Proton Cyclotron @ LNL



New cyclotron: Installed in May 2015, now under commissioning

Dual beam proton cyclotron ($E_p = 35-70$ MeV):

1° - nuclear physics research on RIBs (**SPES project**) : $E=40$ MeV , $I=200$ μ A (upgrade 500 μ A)

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

The LARAMED project

Laboratory of RADionuclides for MEDicine



Double Purposes

- **A research laboratory**, owned jointly by INFN and CNR for:

- Measurement of cross section through targets activation
- High power target tests
- Production of small quantities of experimental radioisotopes (^{99m}Tc , ^{64}Cu , ^{67}Cu , ...)

- **A production facility**, operated by INFN and a private partner, for production of parent radionuclides for $^{82}\text{Sr}/^{82}\text{Rb}$ and $^{68}\text{Ga}/^{68}\text{Ge}$ generator systems

Some INFN project already funded:

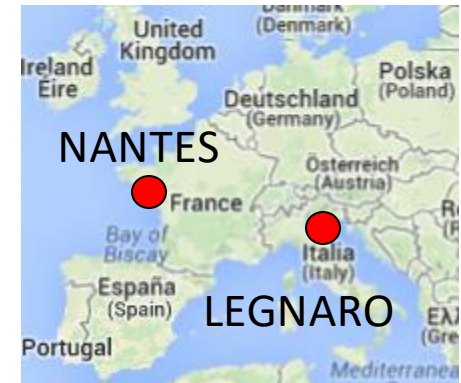
- * APOTEMA and TECHN-OSP, focused on ^{99m}Tc and ^{99}Mo alternative production routes
Participation to CRP concluded in June 2015
(PI: J. Esposito, juan.esposito@lnl.infn.it)
- ** COME, focused on ^{67}Cu production routes
Participation to current CRP
(PI: G. Pupillo, gaia.pupillo@lnl.infn.it)
- *** PASTA (proposal), focused on ^{47}Sc production routes (PI: G. Pupillo)

The LARAMED project: Scientific Collaborations



Waiting for a tested dedicated beam-line and available laboratories, we are collaborating with:

- **ARRONAX facility** (Nantes, France). 70 MeV multi-particle cyclotron
- St. Orsola Hospital (Bologna, Italy). 16 MeV cyclotron routinely used for ^{18}F FDG
- University of Ferrara (Italy). YAP-(S)PET-CT small-animal imaging system
- National Research Council (CNR) in Milan (Italy). Facility for cellular and pre-clinical studies



At LNL we already use γ -spectroscopy laboratory fully equipped with HPGe detectors and technologies for metal vapour deposition, brazing, surface treatment (Material Science Lab.)

Why ^{67}Cu ?

Decay characteristics of ^{67}Cu and ^{64}Cu

Cu-67 61.83 h

β^- : 100 %
(Zn-67)

γ -ray [keV]	γ -ray [%]
184.6	48.7
209.0	0.115
300.2	0.797
393.5	0.220

SPECT

THERAPY					
β energy [keV]	β int [%]	Auger [keV]	Auger [%]		
51	1.1	0.99	19.14		
121	57	7.53	6.87		
154	22.0	83.65	12.09		
189	20.0	Mean β^- : 141 keV			

Copper-67 is very attractive for its physico-chemical characteristics (half-life 2.58 d), suitable for **theranostic applications** (therapy + diagnostic), as single isotope or in pair with ^{64}Cu

Cu-64 12.701 h

ϵ : 61.5 %
(Ni-64)

β^- : 38.5 %
(Zn-64)

γ -ray [keV]	γ -ray [%]
1345.77	0.475

THERAPY	
β energy [keV]	β int [%]
190.70	38.5

β^+
energy
[keV]

β^+ int
[%]

PET

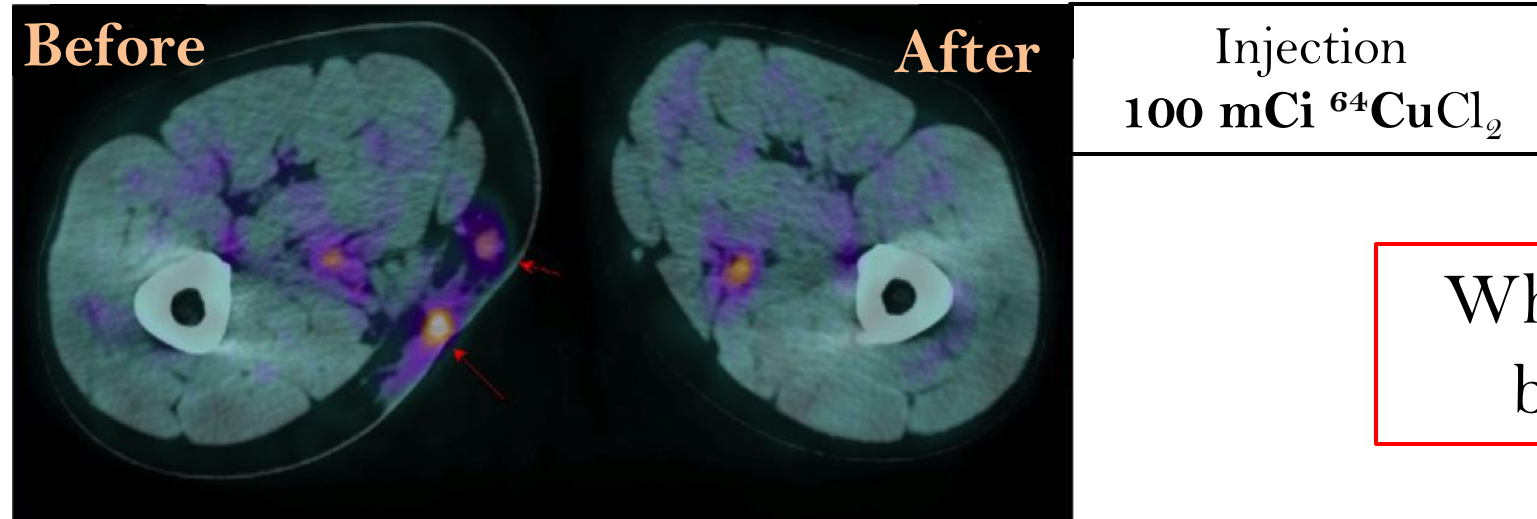
THERAPY	
Auger [keV]	Auger [%]
0.84	57.7
6.54	22.51

The potential of theranostic is the selection of patients prior therapy and the use of personalized doses, based on previous SPECT/CT (^{67}Cu) or PET/CT ($^{67}\text{Cu}/^{64}\text{Cu}$ pair)

NuDat 2.6 database (2013) - NNDC

Applications of ^{67}Cu and ^{64}Cu in medicine

- ^{64}Cu is ALREADY used in nuclear medicine for PET (diagnosis)
- ^{64}Cu seems to provide excellent results also in THERAPY



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

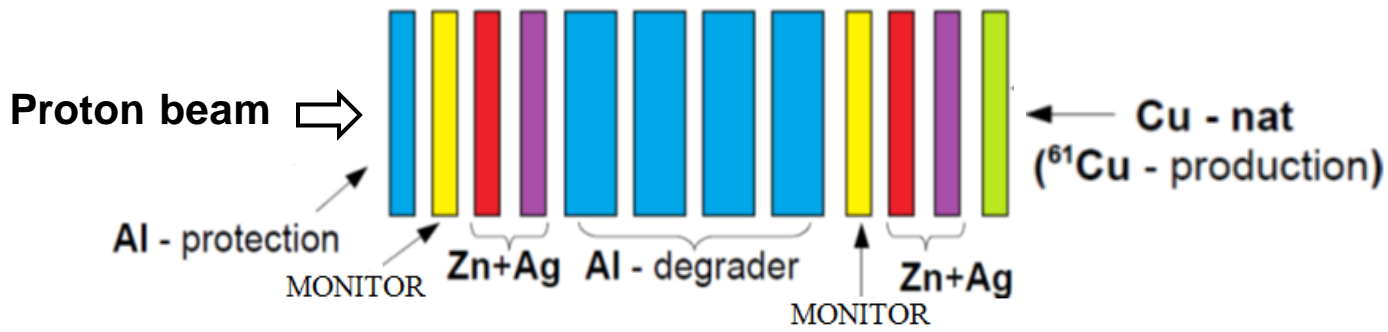
- ^{67}Cu is a promising nuclide in RAdio Immuno Therapy (RAIT)
- ^{67}Cu 's limiting factor: LOW availability

Worldwide Production per month : only 1 patient dose (100 mCi \approx 3.7 GBq) 

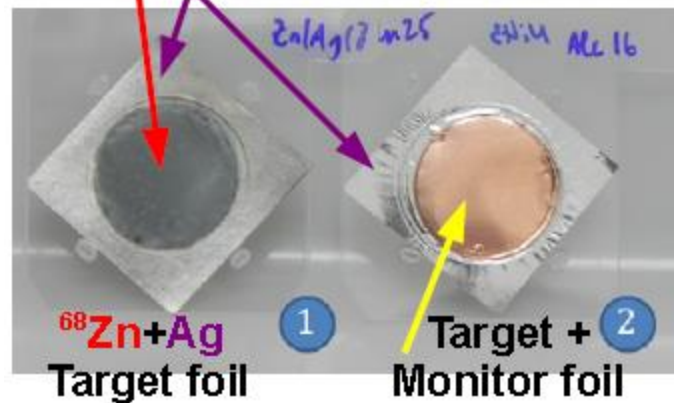
\rightarrow ^{67}Cu production: Goal for LARAMED and ARRONAX !

The $^{68}\text{Zn}(p,2p)^{67}\text{Cu}$ cross section at ARRONAX facility

Stacked-foil target structure



Target foil(s):
 ^{68}Zn Electrodeposition ($\sim 10\mu\text{m}$)
 Ag Support ($\sim 25\mu\text{m}$)



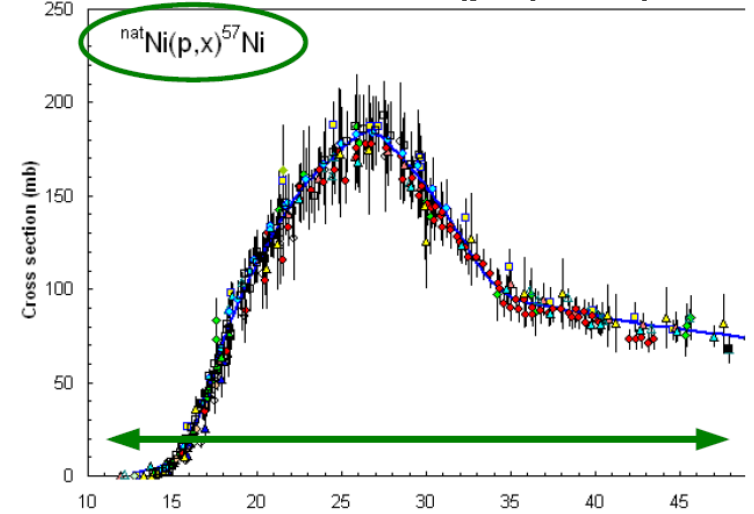
Stacked-foil Target holder



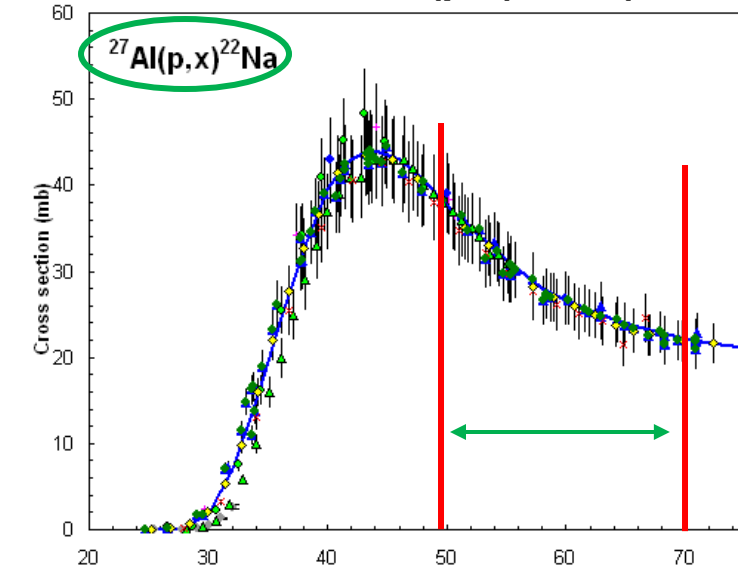
* International Atomic Energy Agency (IAEA)
http://www-nds.iaea.org/medical/monitor_reactions.html

Monitor reactions*:

$E_p < 50 \text{ MeV} \rightarrow \text{natNi}(p,x)^{57}\text{Ni}$ ($\text{natNi} \sim 20 \mu\text{m}$)

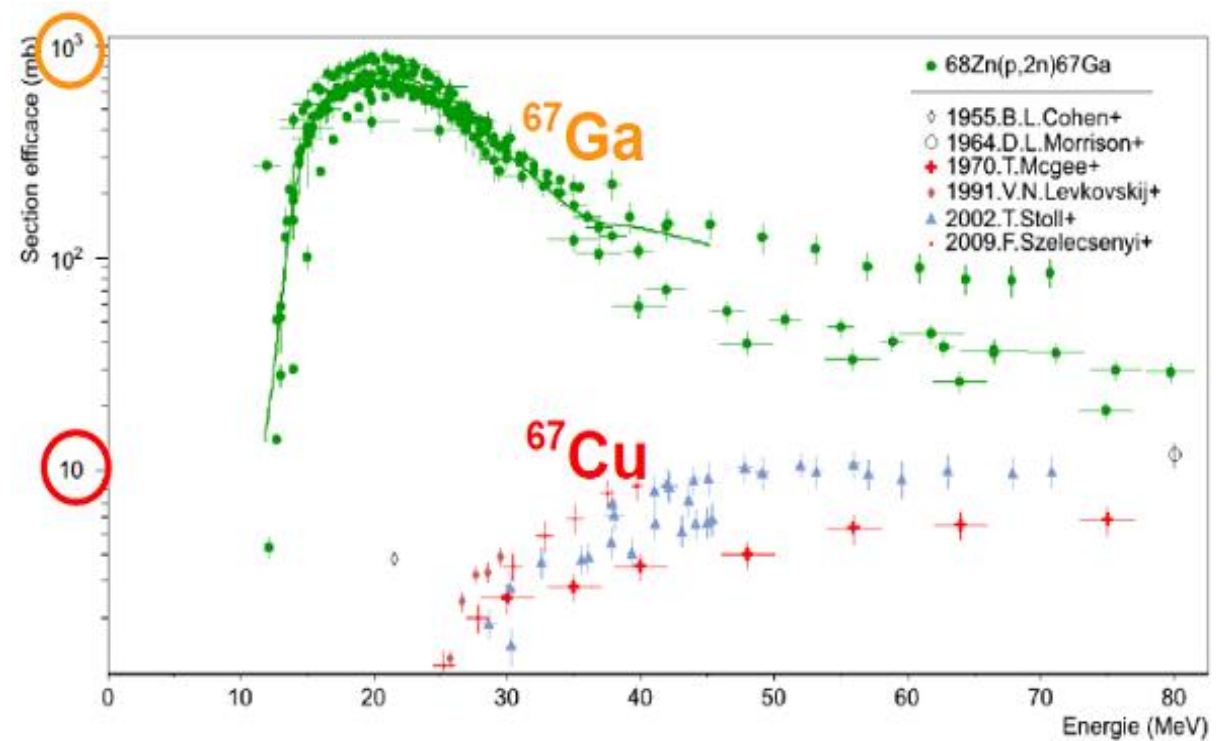


$E_p > 50 \text{ MeV} \rightarrow ^{27}\text{Al}(p,x)^{22}\text{Na}$ ($^{27}\text{Al} \sim 20 \mu\text{m}$)



$^{68}\text{Zn}(p,x)$ reactions: co-production of ^{67}Cu and ^{67}Ga

Energy [keV]	Cu-67 Intensity	Ga-67 Intensity
91.266 5	7.0 1	3.11 4
93.311 5	16.1 2	38.81 3
184.577 10	48.7 3	21.41 1
208.951 10	0.115 5	2.46 1
300.219 10	0.797 11	16.64 12
393.529 10	0.220 8	4.56 24
494.166 15		0.0684 14
703.106 15		0.0105 9
794.381 15		0.0540 18
887.688 15		0.148 3

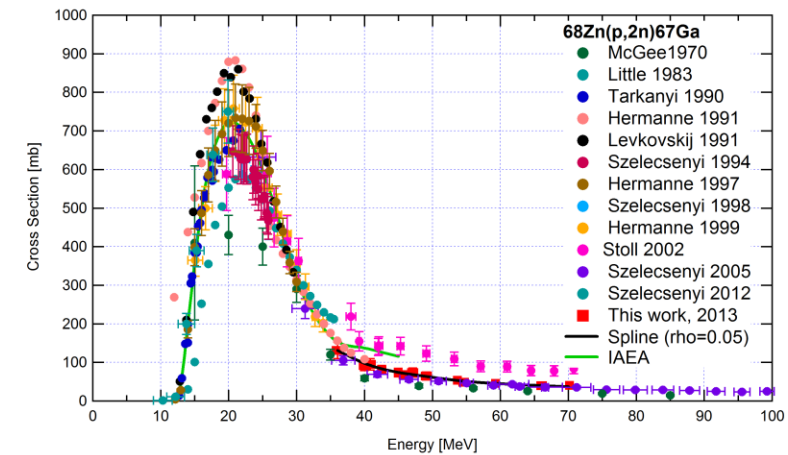
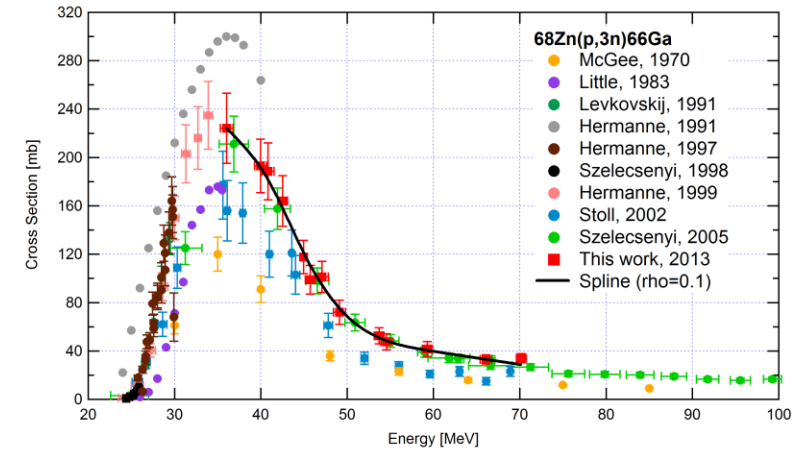
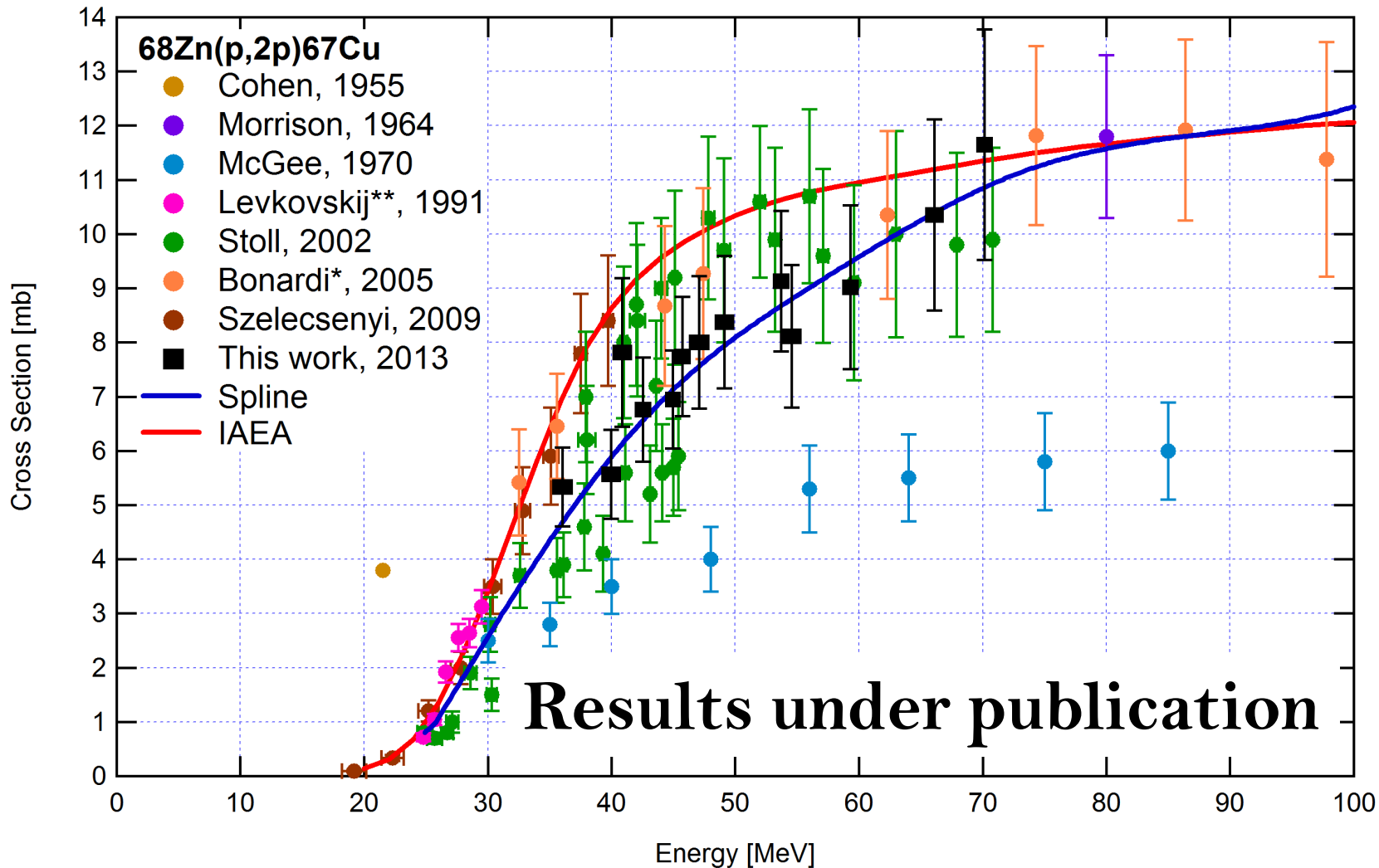


^{67}Cu ($t_{1/2}$ 61.83 h) ^{67}Ga ($t_{1/2}$ 78.24 h)



Chemical separation Cu/Ga is mandatory !!
Tracer: **Cu-61** and **Ga-66**

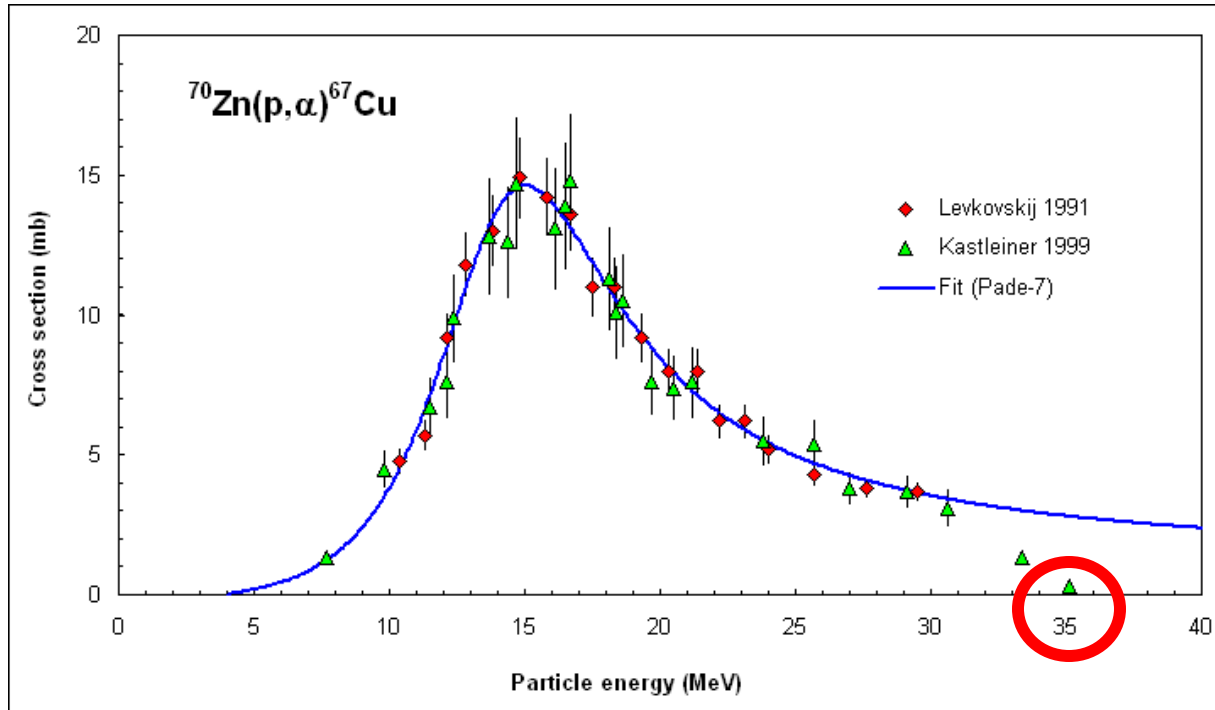
The $^{68}\text{Zn}(p,2p)^{67}\text{Cu}$ cross section measurement



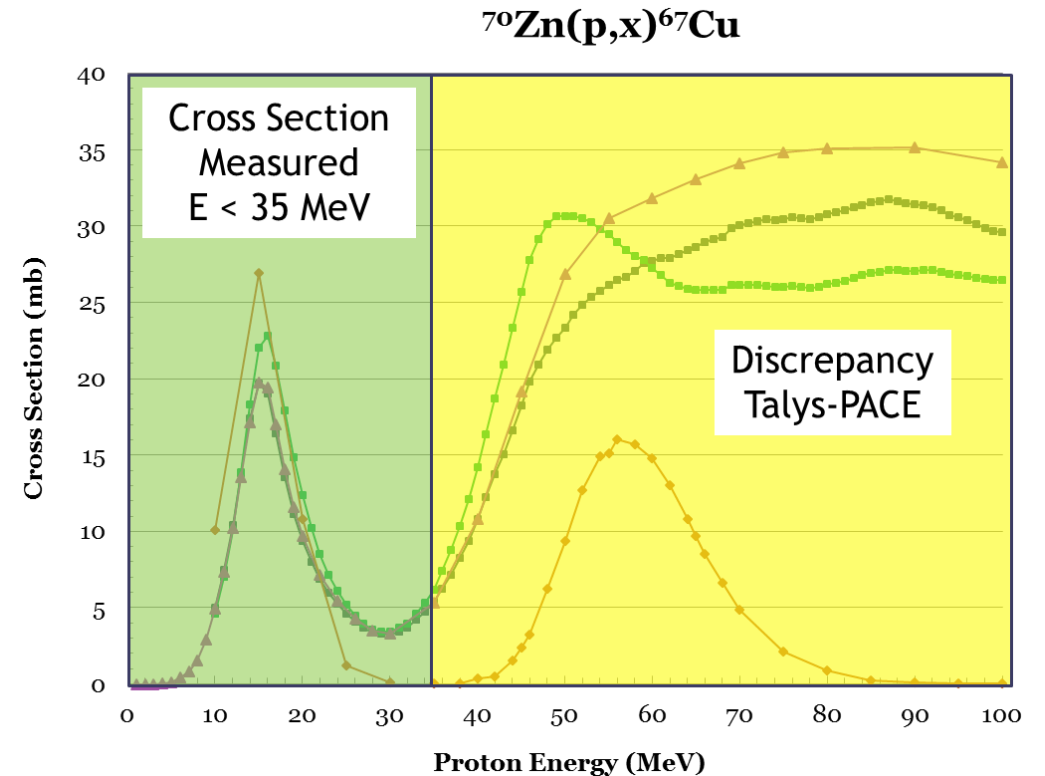
The project COME
COpper Measurement
CSN3 - LNL - 2016



COME project: Alternative production route of ^{67}Cu



IAEA, <https://www-nds.iaea.org/radionuclides/emerging.html>



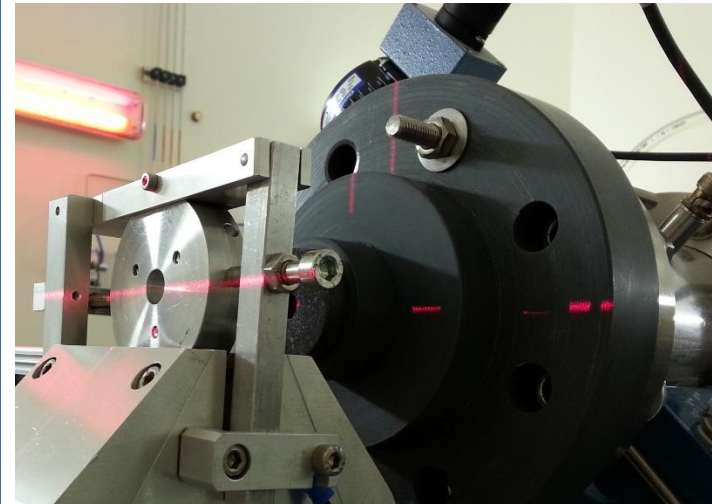
We need the support of nuclear physics community to explain this disagreement !

➤ **Accurate measurement of this reaction in progress @ Arronax !**

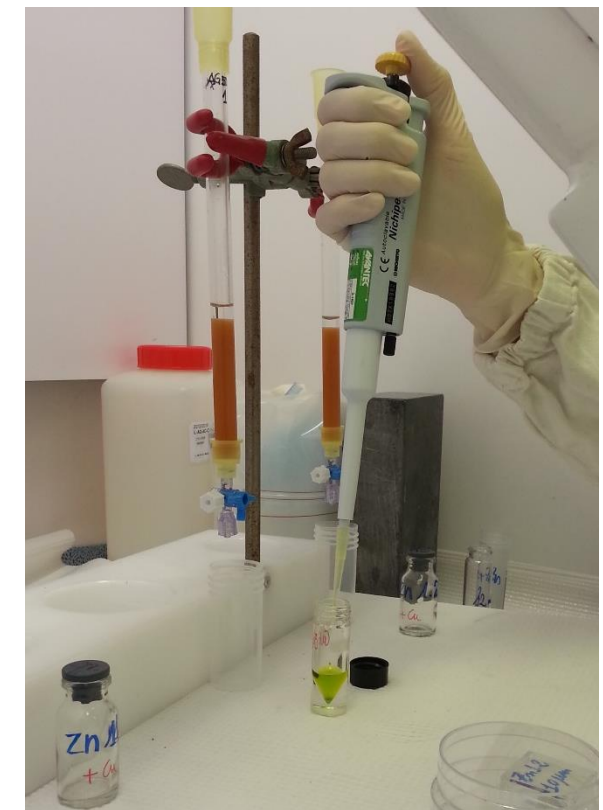
COME project: Alternative production route of ^{67}Cu



Collimator in graphite and its support (L) ; target-holder (R)
Realized @ LNL

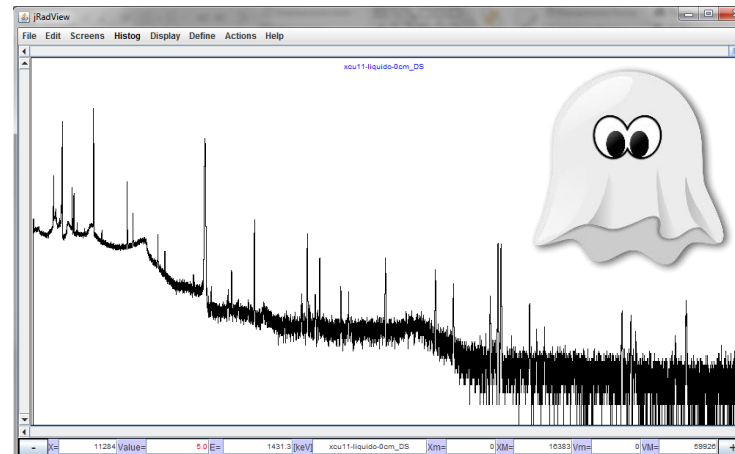


Alignment of collimator and target-holder on the beam-line @ Arronax



Development and realization of radiochemical process @ Arronax

	Irradiation run	Ep (MeV)	Time irr. (s)	Mean current (nA)
1	23/02/2016	70.3	5390	98.8
2	06/04/2016	56.0	5396	100.4
3	10/05/2016	61.0	4895	110.5
4	07/06/2016	68.0	5406	100.7
5	20/06/2016	48.0	7270	102.5



**Data Analysis
Ongoing ..**

Irradiation runs @ Arronax

(Nantes, France, IBA cyclotron 70 MeV)



1^o Meeting of the Coordinated Research Project (CRP) organised by IAEA
**Therapeutic Radiopharmaceuticals Labelled with New Emerging
Radionuclides (^{67}Cu , ^{186}Re , ^{47}Sc) – Wien , 5-10 Sept. 2016**



Thank you for your attention!

