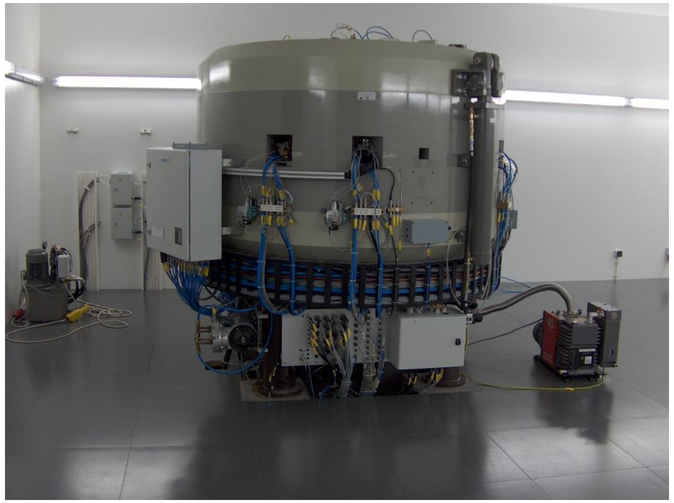
ICNAS

Institute for Nuclear Sciences Applied to Health

University of Coimbra – Portugal

15 years of acceleration



ICNAS: *from molecules to man*

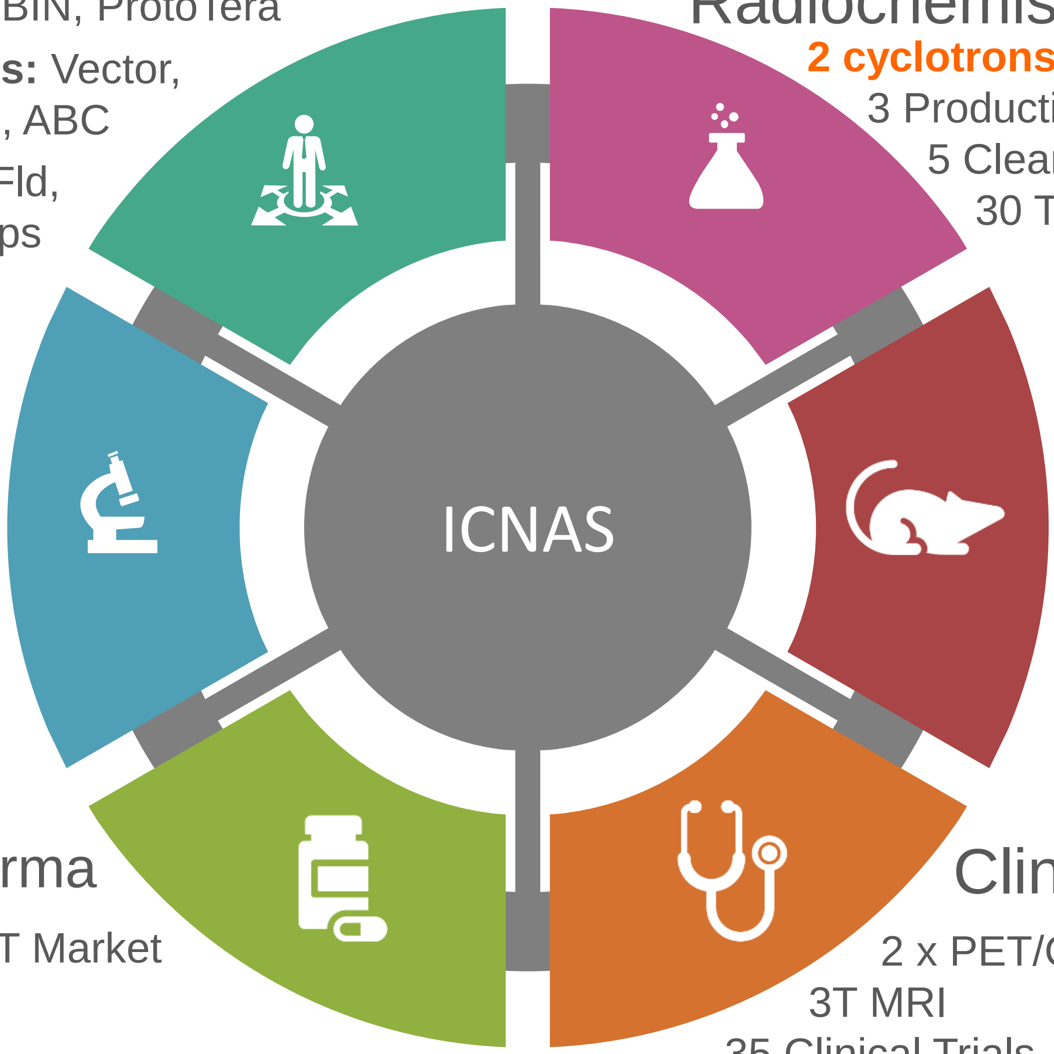
GLP GMP GCP

Networks: BIN, ProtoTera

CoLabs: Vector, HealthyAgeing, ABC

Spin-offs: Fld, braineyes, Cyclops

Ass. Labs: LASI



Radiochemistry

2 cyclotrons
3 Production labs
5 Clean Rooms
30 Tracers / 7 nuclides

Preclinic

MRI/MRS/fMRI
Micro-PET
SPECT
PAT
Optical
Labs

CIBIT

45 researchers
30+12 PhD students

ICNAS Pharma

7 products in PT Market
1 in Spain

Clinic

2 x PET/CT
3T MRI
35 Clinical Trials

IAEA
International Atomic Energy Agency
Institute for Nuclear Sciences Applied to Health
University of Coimbra (ICNAS)
IAEA Collaborating Centre
for
Production and R&D of Radioisotopes and Radiopharmaceuticals
2020 – 2024

EURO BIOIMAGING

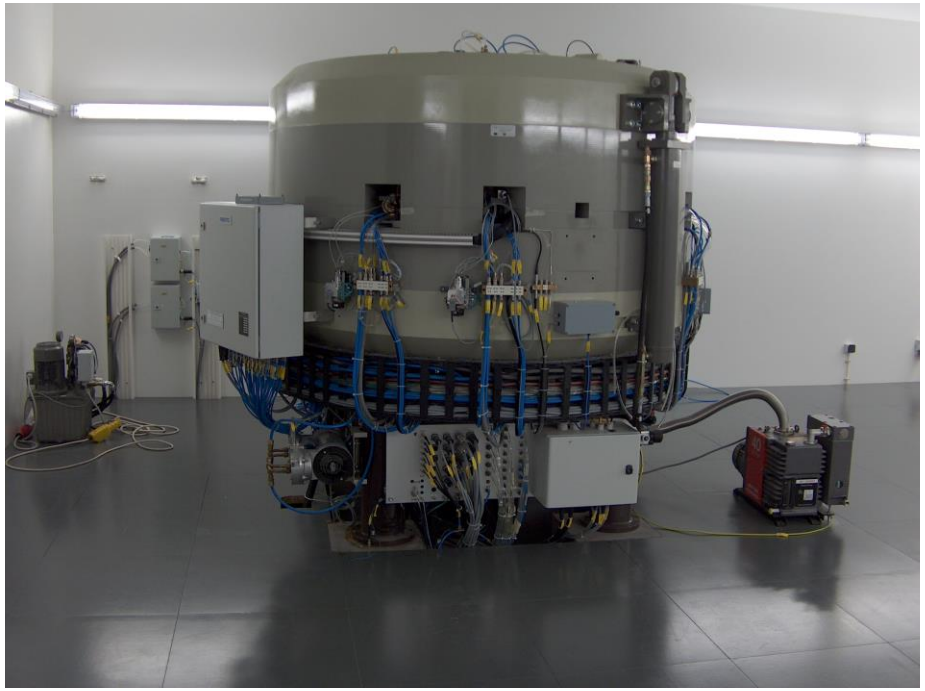
edqm

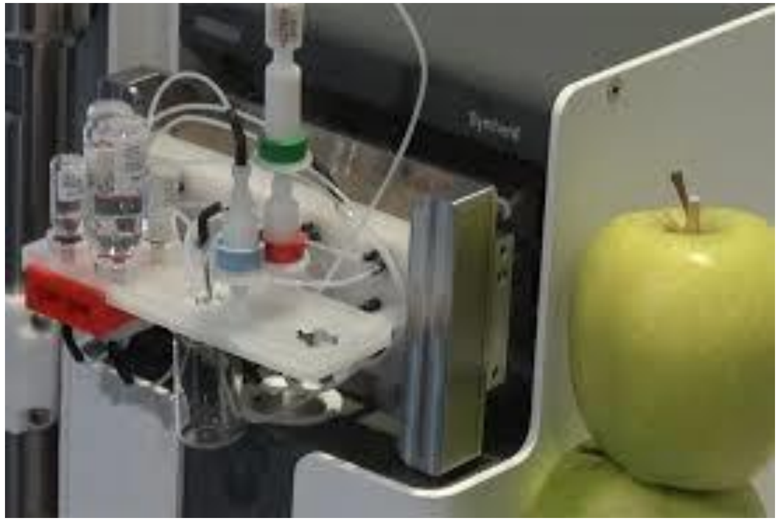
NOAR
NETWORK FOR OPTIMIZED ASTATINE LABELED RADIOPHARMACEUTICALS

EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

iba | Academy

In the beginning…





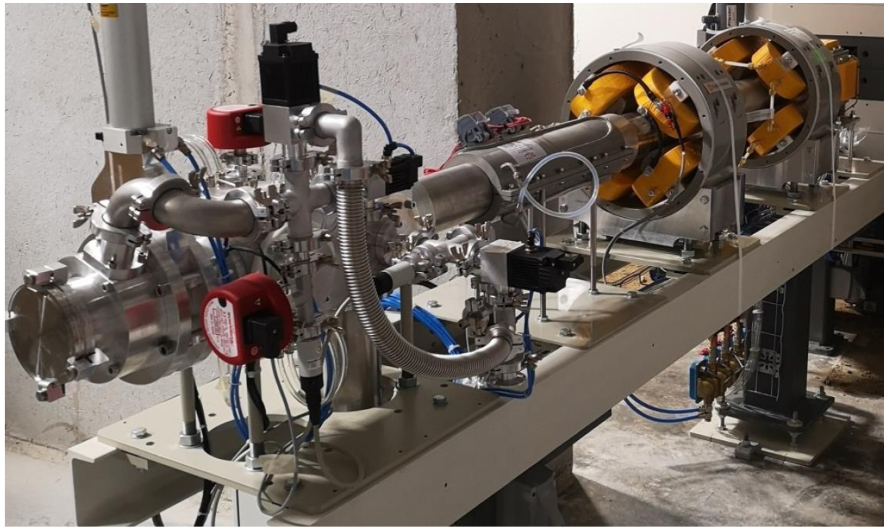
In the beginning…

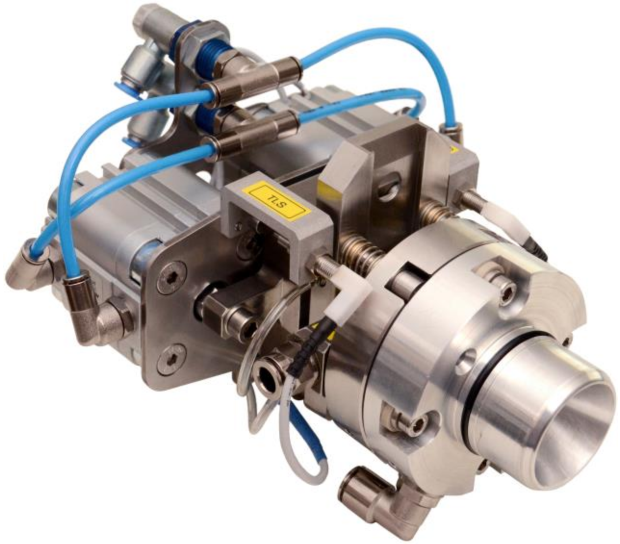
^{68}Ga on demand; dotanoc labelling

but…

Generators : increasingly expensive… limited availability… limited elutions…

classic approach: solid targets





high production amounts… but special infrastructure and targets required…

so… what about a liquid target?...

existing infrastructure, setups and experience… enough amounts for clinic use!

^{68}Ga on demand : production every hour

the new paradigm: production of radiometals using liquid targets

Production of ^{68}Ga

(specifically customized) Niobium target

- $^{68}Zn(p,n)^{68}Ga$
- Havar + Nb window => E ≈ 14 MeV
- 200 mg of Zinc-68 dissolved in nitric acid (vol≈ 3 ml)
- 1 hour irradiation time, “like-F18” conditions
- 200 mCi of ^{68}Ga

production of 68Ga using liquid targets in cyclotrons: the difficulties

METAL CONTAMINATION : purity of ^{68}Zn ; (quality) preparation of the solution

^{67}Ga ISOTOPIC IMPURITIES

avoid $^{67}Zn(p,n)\,^{67}Ga$: **enrichment of ^{68}Zn**

avoid $^{68}Zn(p,2n)\,^{67}Ga$:

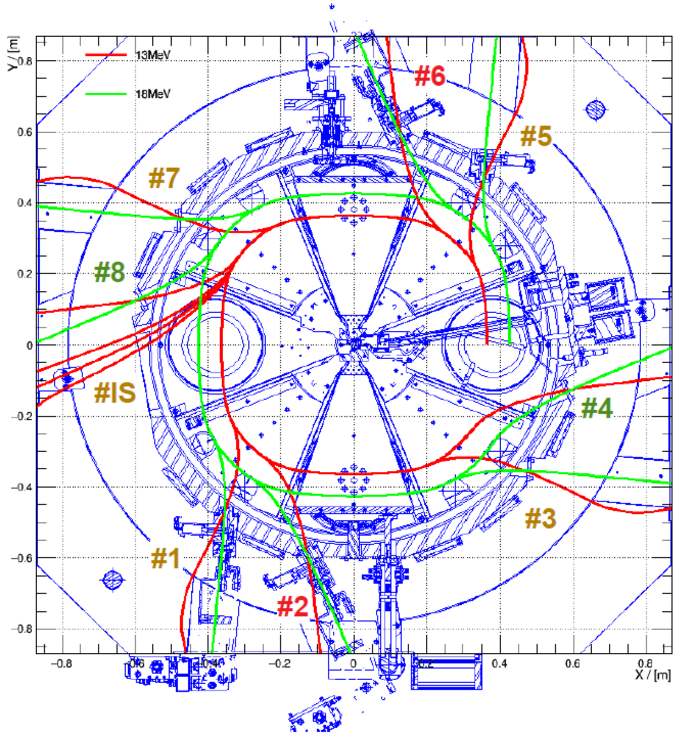
lower proton **beam energy** on target

$^{68}Zn(p,2n)\,^{67}Ga$ vanishes at E< ~12 MeV

a new paradigm… leading to new ideas!

A dual energy cyclotron: 18 MeV + other to be chosen in the range [18-13] MeV

R&D joint project ICNAS & IBA



a new paradigm… leading to new ideas! ^{61}Cu

Table 5. Proton-induced nuclear reactions occurring in ^{68}Zn-enriched zinc and theoretical productions yields for a typical irradiation with 14.2 MeV protons impinging on 3 ml of target solution with a 200 mg of ^{68}Zn.

Zinc nuclide (abundance in ^{nat}Zn)	Abundance (%)	Nuclear reaction	Decay: Half-life	Decay: β^- (MeV)	Decay: β^+ (MeV)	Decay: EC (%)	Decay: γ-rays (keV)	Theoretical yield ($MBq/\mu A_{sat}$)	Cross-section references	Activity@EOB (MBq) for a 1 h long irradiation with 50 μA
^{64}Zn 48.6%	0.01	$^{64}Zn(p,\alpha)^{61}Cu$	3.33 h		1.215 (61.5%)	38.5	283 (12.0%) 511 (123%) 656 (10.4%)	4.15E-03	67, 77	0.039
		$^{64}Zn(p,pn)^{63}Zn$	32.4 s				669.6 (8%)			
		$^{64}Zn(p,\gamma)^{65}Ga$	15.2 min				115.09 (54%) 751.8 (8.1%)	4.44E-05	78, 79	2.08E-03
		$^{64}Zn(p,n)^{64}Ga$	2.63 min				807.8 (14.54%) 991.6 (46%)			
^{66}Zn 27.9%	0.01	$^{66}Zn(p,n)^{66}Ga$	9.49 h		4.153 (56.0%)	44	511 (114%) 833 (5.9%) 1039 (37%) 2190 (5.3%) 2751 (22.7%)	0.037	60, 67, 80	0.130
		$^{66}Zn(p,2n)^{65}Ga$	15.2 min					0	67	0
		$^{66}Zn(p,pn)^{65}Zn$	244.0 days		0.33 (1.42%)	98.6	1115 (50.23%)	3.95E-04	60, 67, 81	2.34E-06
^{67}Zn 4.1%	0.3	$^{67}Zn(p,n)^{67}Ga$	3.26 days			100	93.3 (70.6%) 184.6 (21.3%) 300.2 (16.67%)	1.222	60, 82	0.539
		$^{67}Zn(p,\alpha)^{64}Cu$	12.7 h	0.579 (38.5%)	0.653 (17.52%)	43.5	511 (35.04%) 1346 (0.475%)	5.68E-02	67	0.151
		$^{67}Zn(p,2n)^{66}Ga$	9.49 h		4.153 (56%)	44	511 (114%) 833 (5.9%) 1039 (37%) 2190 (5.3%) 2751 (22.7%)	9.31E-03	60, 67, 81	0.0328
^{68}Zn 18.8%	99.5	$^{68}Zn(p,n)^{68}Ga$	67.8 min		1.899 (88.9%)	11.1	511 (178%) 1077 (3.24%) 1883 (0.142%)	599.0	60, 67, 80	13732.9
		$^{68}Zn(p,2n)^{67}Ga$	3.26 days			100	93.3 (70.6%) 184.6 (21.3%) 300.2 (16.67%)	23.2	60, 82	10.23
		$^{68}Zn(p,n\alpha)^{64}Cu$	12.7 h	0.579 (38.5%)	0.653 (17.52%)	43.5	511 (35.04%) 1346 (0.475%)	2.31	16	6.12
^{70}Zn 0.6%	0.18	$^{70}Zn(p,\alpha)^{67}Cu$	2.58 days	0.577 (100%)			184.6 (48.7%)	9.39E-03	67, 83	5.24E-03
		$^{70}Zn(p,n)^{70}Ga$	21.14 min	1.656 (99.6%)		0.41	176 (0.29%) 1039 (0.65%)		84	
		$^{70}Zn(p,pn)^{69}Zn$	56.4 min	0.906 (100%)			319 (0.0012%)	2.72E-03	67	0.071

the new paradigm… leads to new ideas! ^{61}Cu

	^{64}Cu	^{61}Cu
Target material	enriched ^{64}Ni	natural Zn
Half-life	12,7 h	3,3 h
Decay properties	17,52 % β^+	61,5 % β^+ / no β^-

Table 2 Activities produced after a typical 45 min long irradiation of natural Zn

Nuclide	Activity produced EOB (MBq)	(Percentage from calculated predictions)
^{61}Cu	271.9	68.8
^{66}Ga	344.8	48.1
^{67}Ga	22.4	69.6
^{68}Ga	2209.5	46.4
^{65}Zn	0.225	103.3
^{64}Cu	n.a	n.a

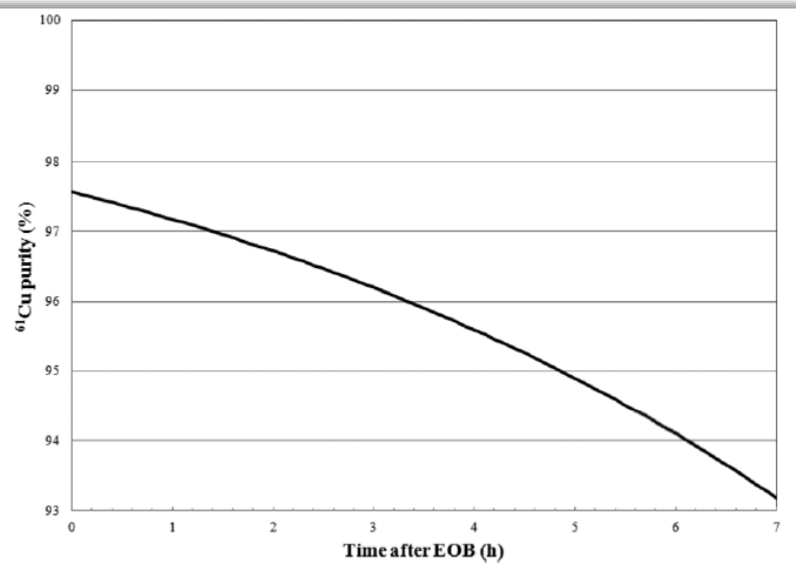
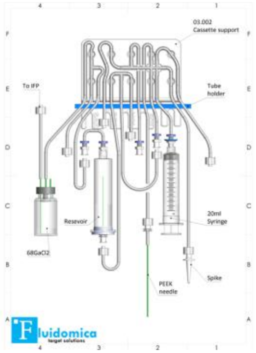


Fig. 2 Experimentally deduced purity of the ^{61}Cu produced as a function of time after EOB.

2 hours irradiation of 99% enriched ^{64}Zn ⇒ **50 mCi of ^{61}Cu**

the new paradigm: production of radiometals using liquid targets

Liquid target



Single use kits and specific purification

GMP compliant automated process

Copper-64

- **$^{64}Ni(p,n)^{64}Cu$**
- **100 mg ^{64}Ni, 5h irradiation: 100 mCi ^{64}Cu**

Zirconium-89

- **$^{89}Y(p,n)^{89}Zr$** E ≈ 14 MeV
- **1 g of ^{89}Y; 4h irradiation: 10 mCi of ^{89}Zr**

routine production @ ICNAS: 18th February 2021

50mCi
(Feb 2020)

50mCi
(Jun 2020)

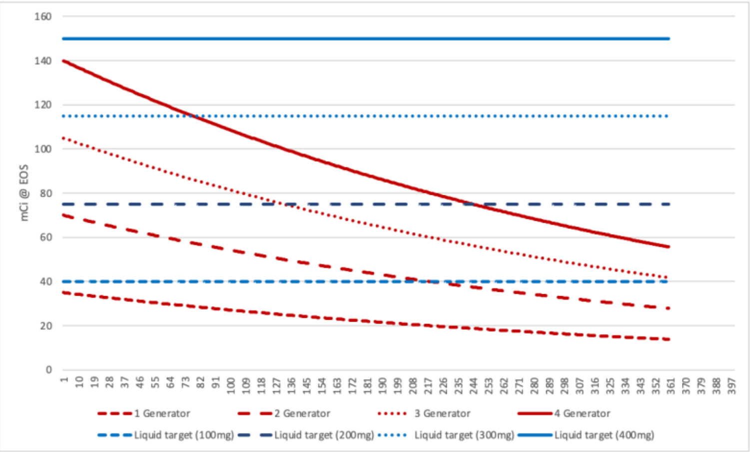
50mCi
(Dec 2020)

^{68}Ga [eluted] (mCi)
53.63

Limited to secular decay

(number of elutions/day)

3 generators = 200+ k€ …



Or…

13 MeV beam

^{68}Ga [End Of Purification] (mCi)
115.52

1 production run

on-demand unlimited production (one per hour)

amount of starting ^{68}Zn target material chosen on demand

versatile & reproducible runs

medium term huge savings

our secret ?… good liquids !

Thank you !