From the Production of Radioisotopes to the Precision Dispensing of Radiopharmaceutical Injections: the Complete Spectrum

RADIOPHARMA

Mario Malinconico

Product Manager & Senior Radiochemist

COMECER

AN ATS COMPANY

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THAI MEDICAL PHYSICIST SOCIETY

WHO IS COMECER

We develop and manufacture high-tech systems necessary for Aseptic Processing and Containment.

Our equipment is used by pharmaceutical companies, radiopharmacy departments, regenerative medicine and tissue engineering organizations worldwide.

We believe in Safety first for operators, patients and products.

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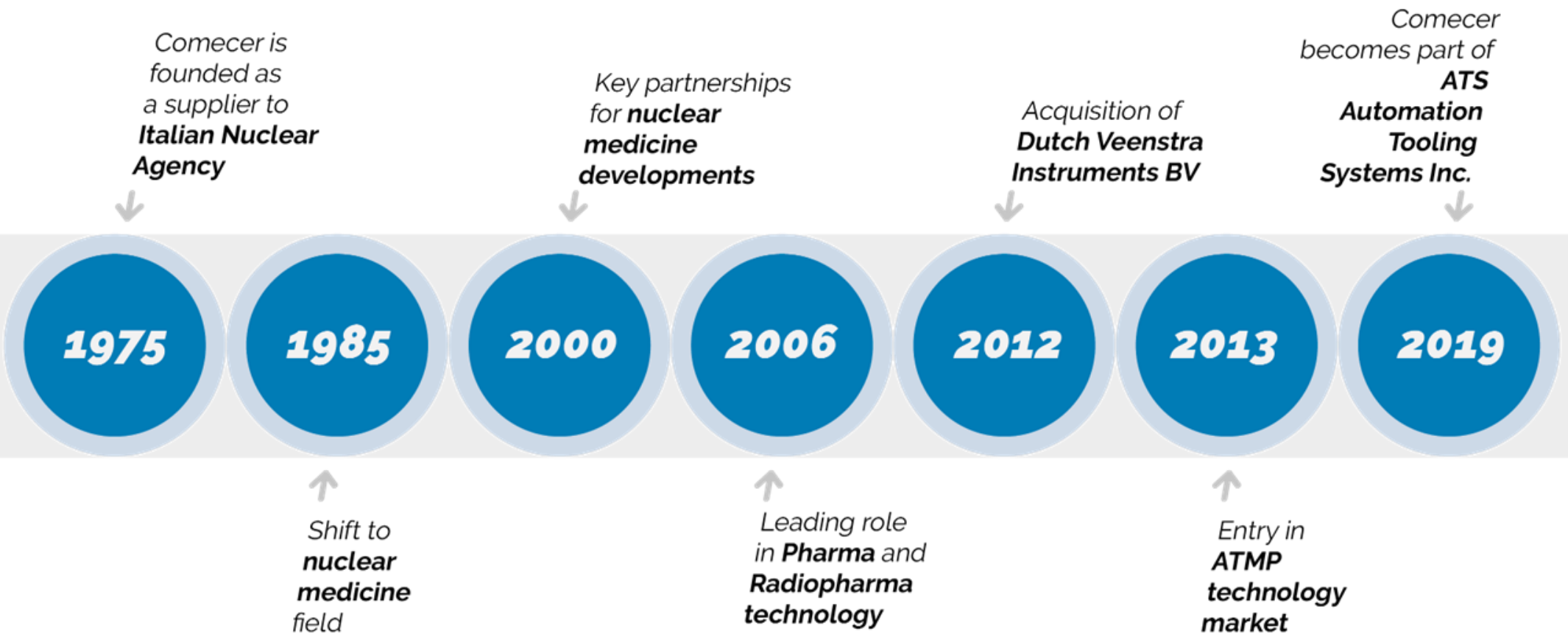
MORE THAN 40 YEARS EXPERIENCE



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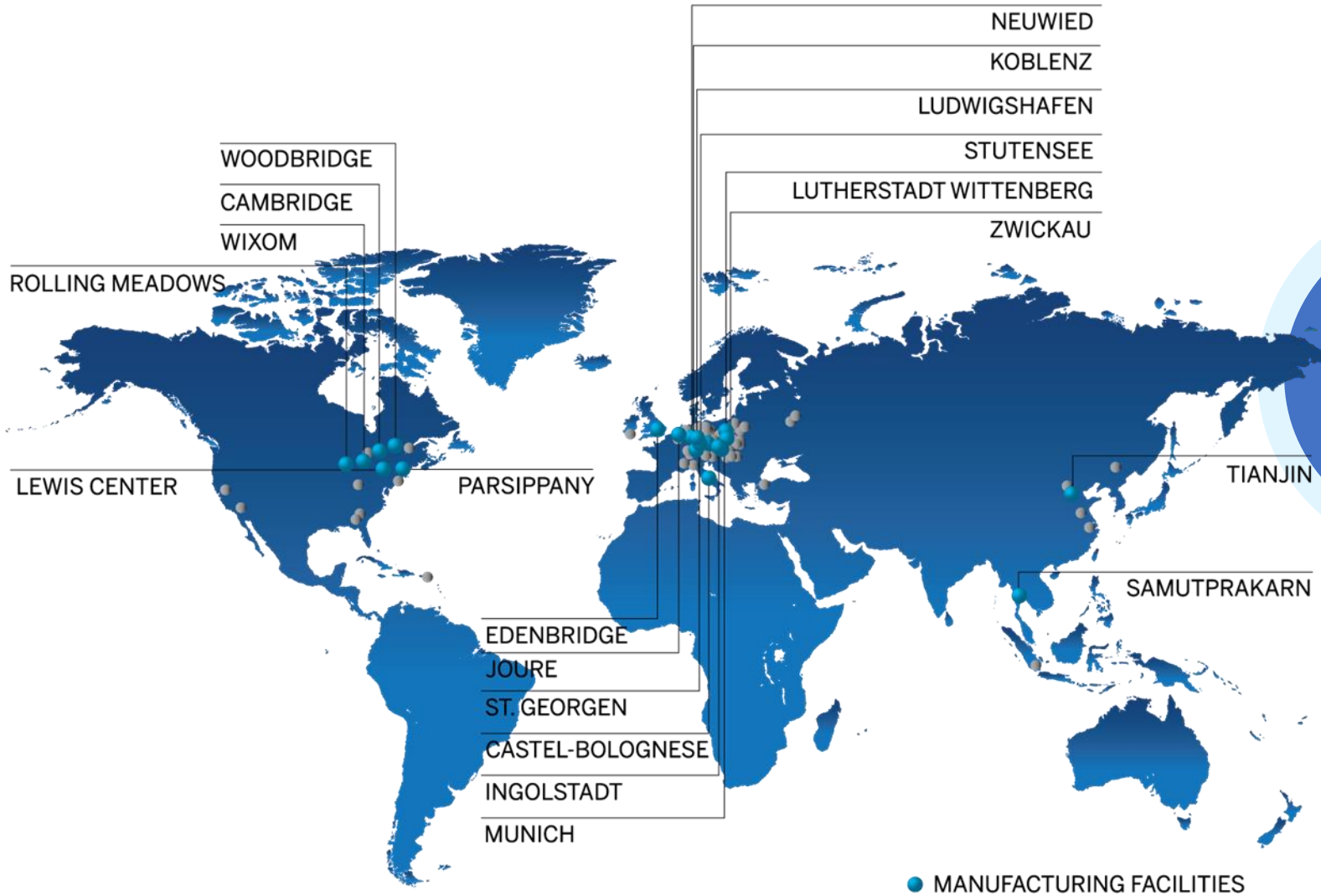
PROUD TO BE PART OF ATS GROUP



22 *COUNTRIES*

4.400+ *EMPLOYEES WORLDWIDE*

50+ *OFFICES*

20 *FACILITIES*

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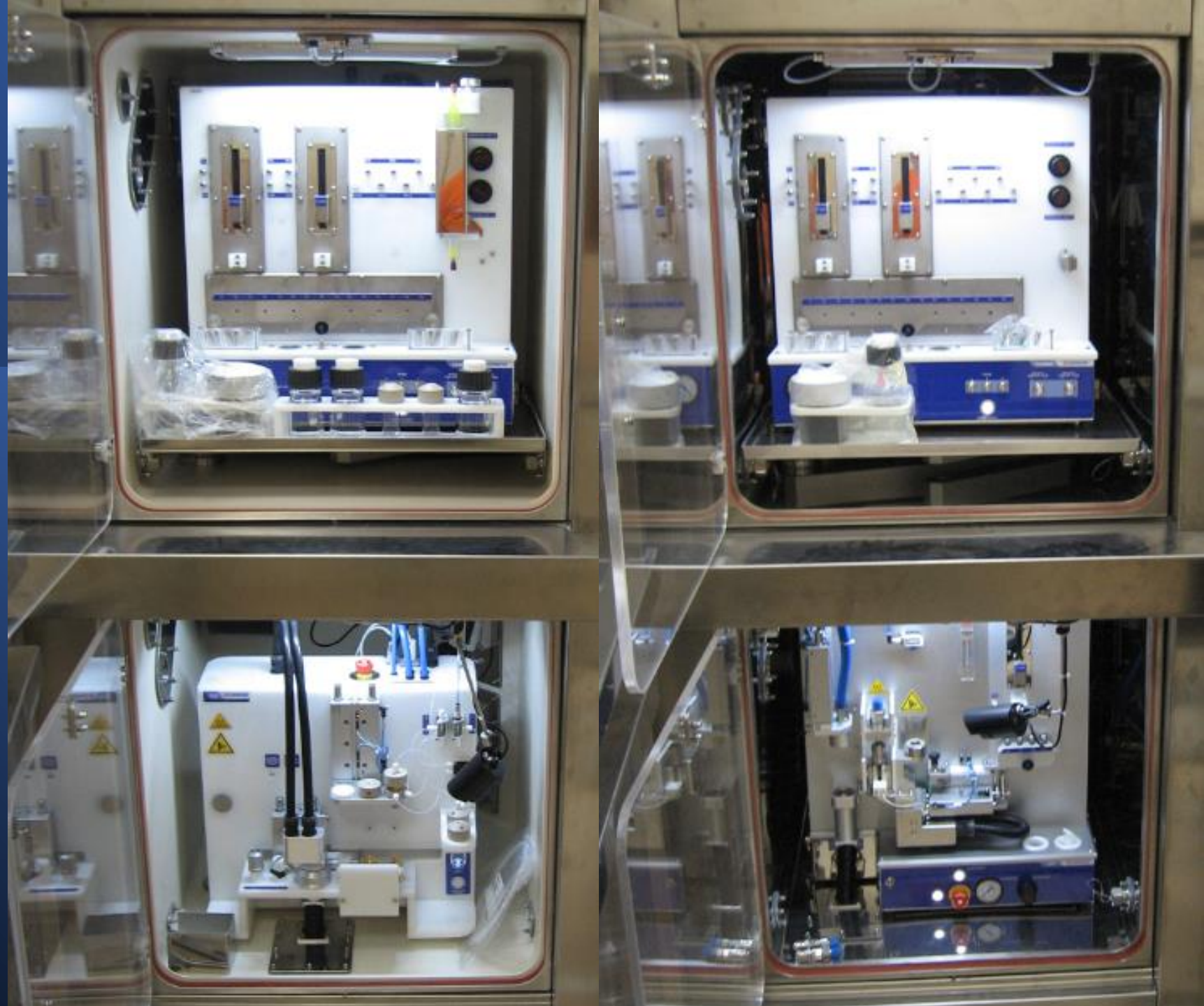
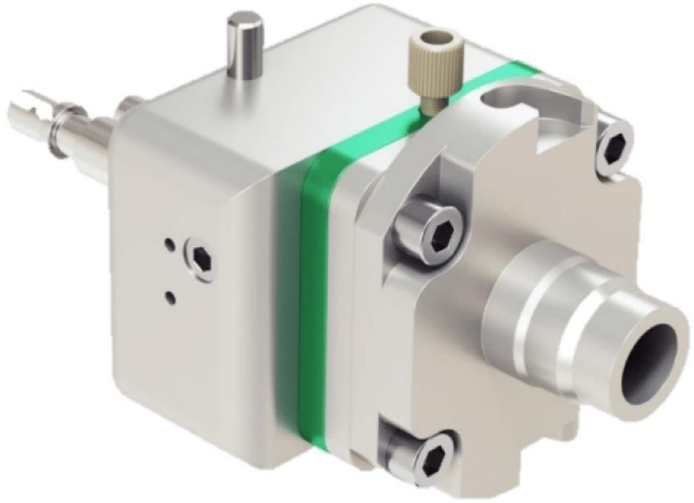
Overview of 68Ga life cycle: a case study

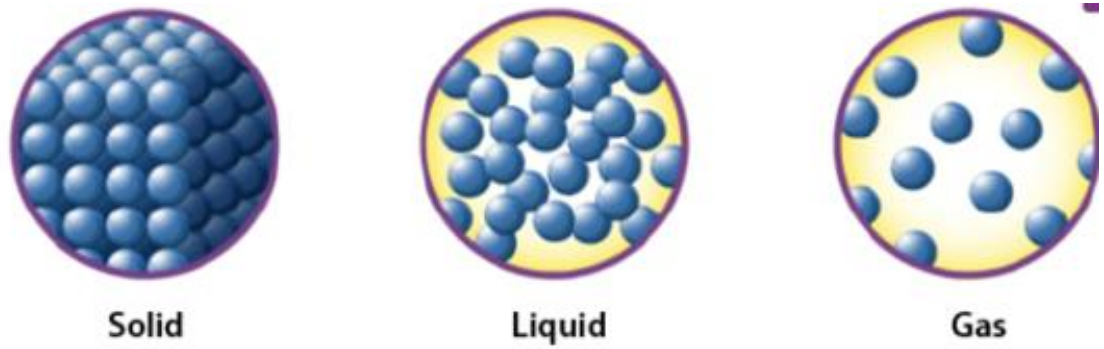
Radioisotope production



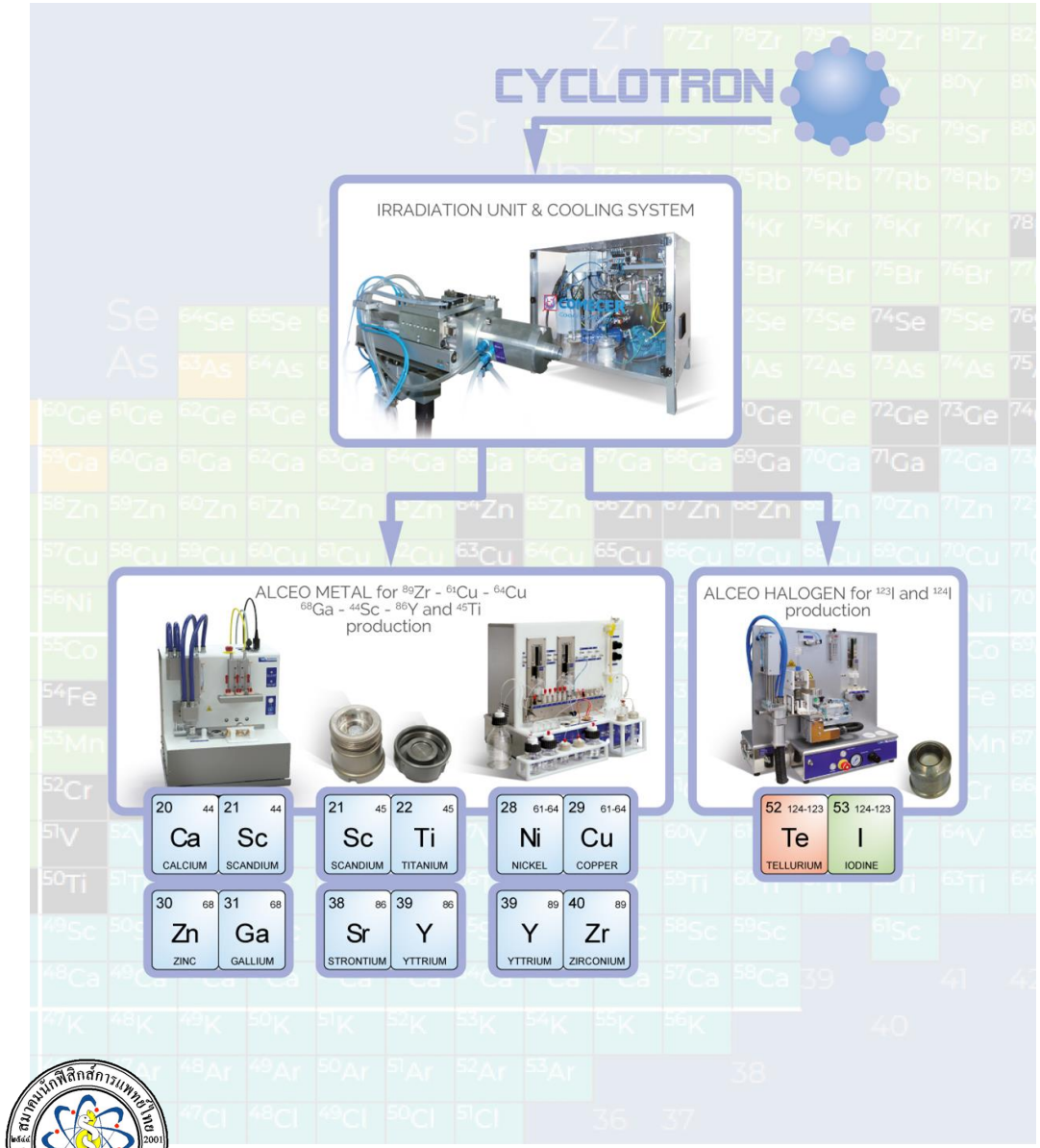
Why a solid target?



The atom density of the target species in the target material—e.g., a solid or liquid might provide higher atom densities than a gas and thus produce greater amounts of the desired product.



Alceo 4.0: solid target processing system configurations



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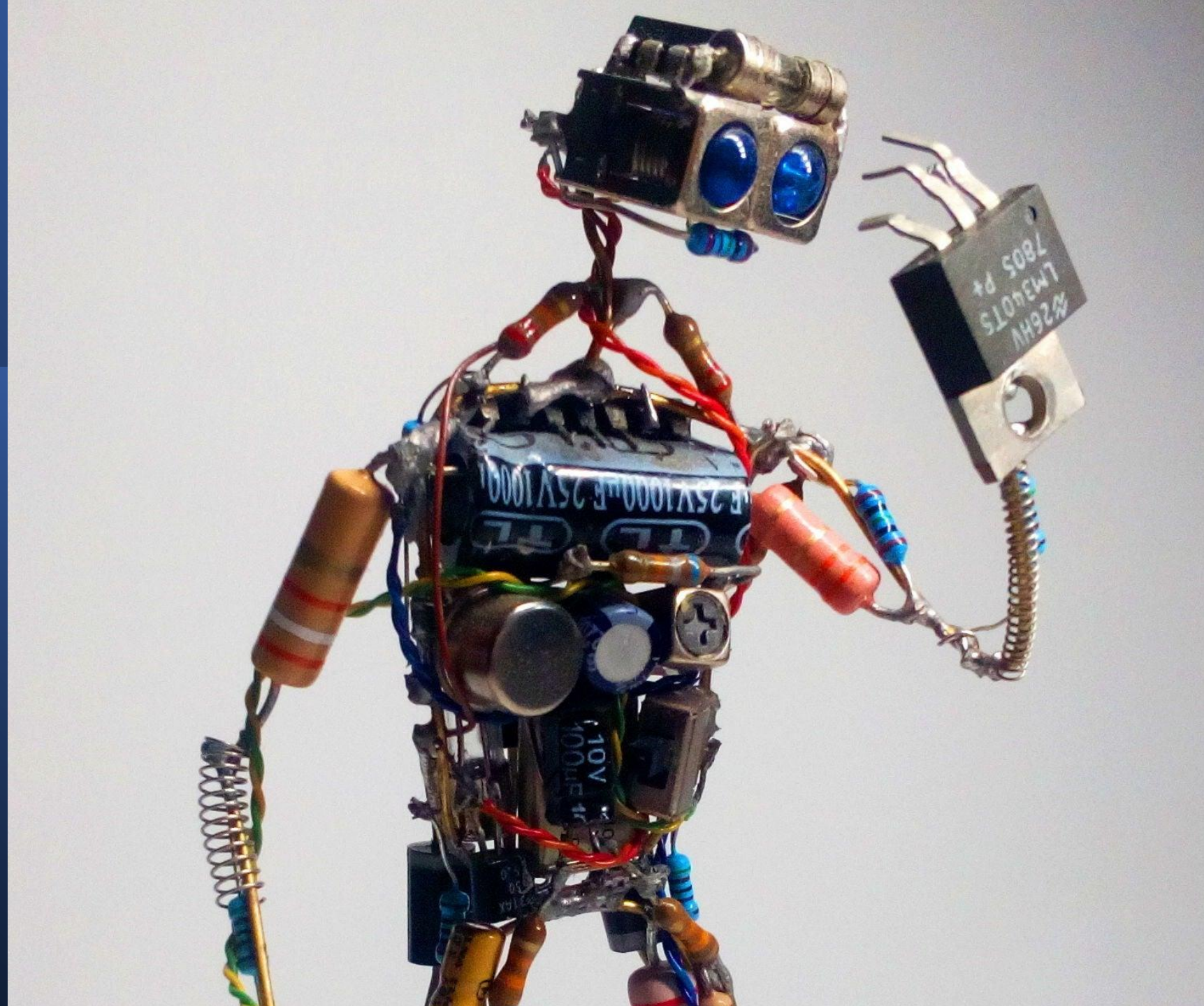
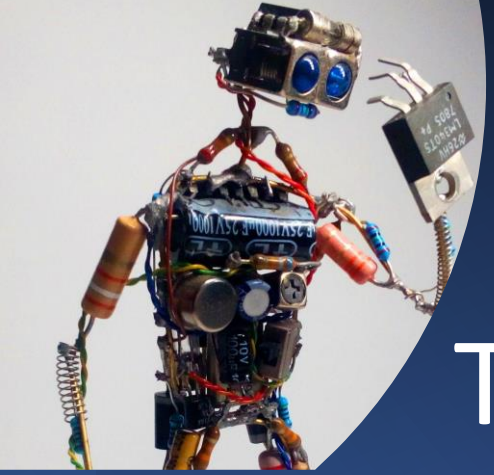
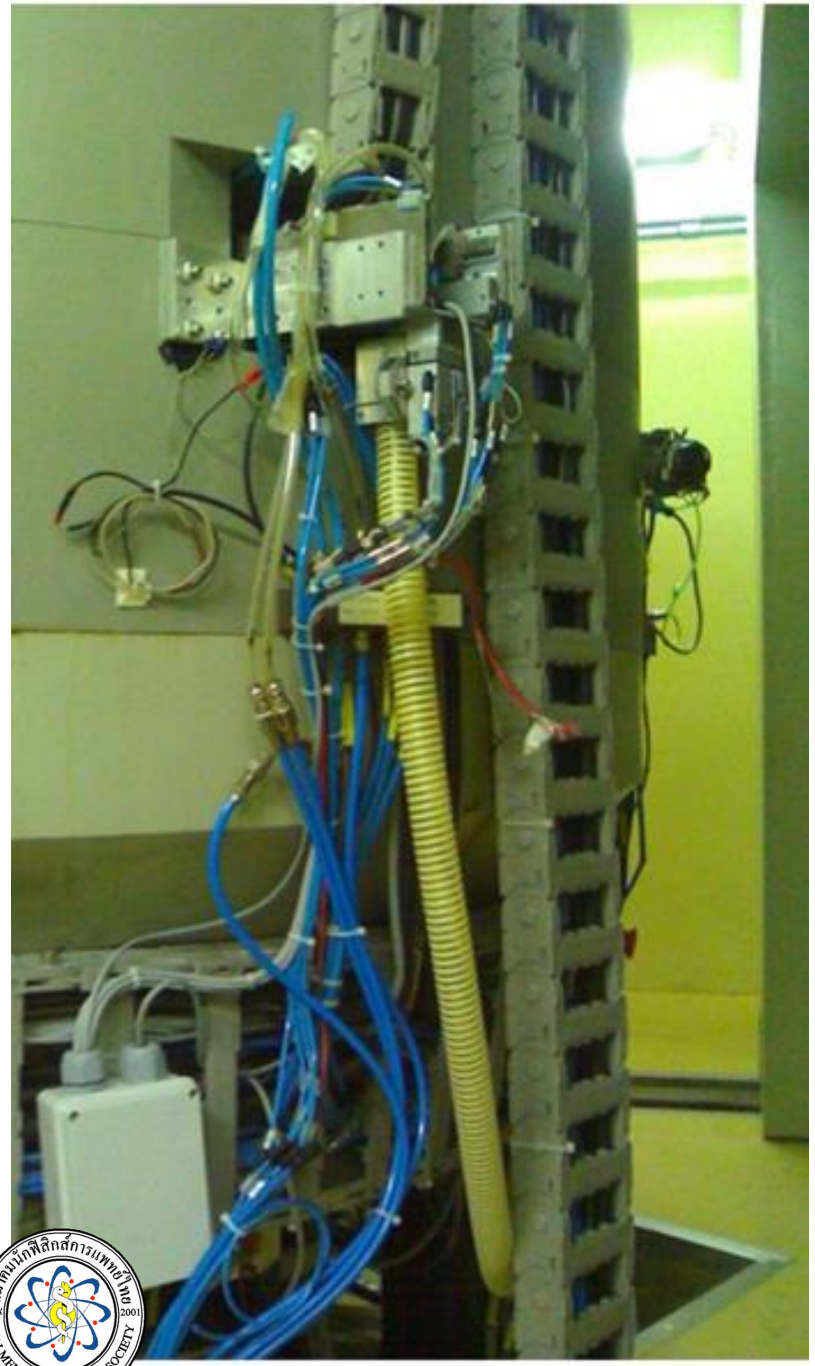
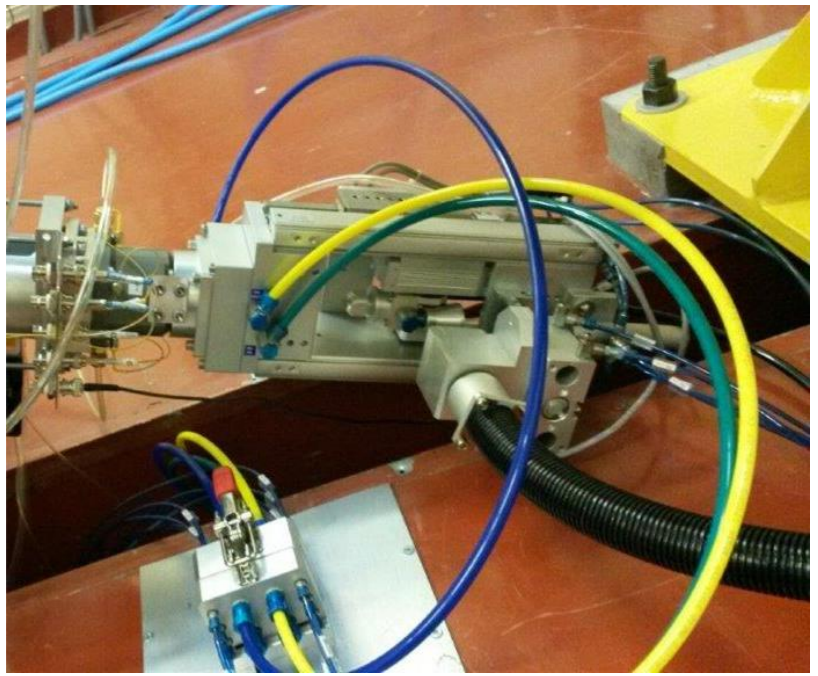
COMPONENTS

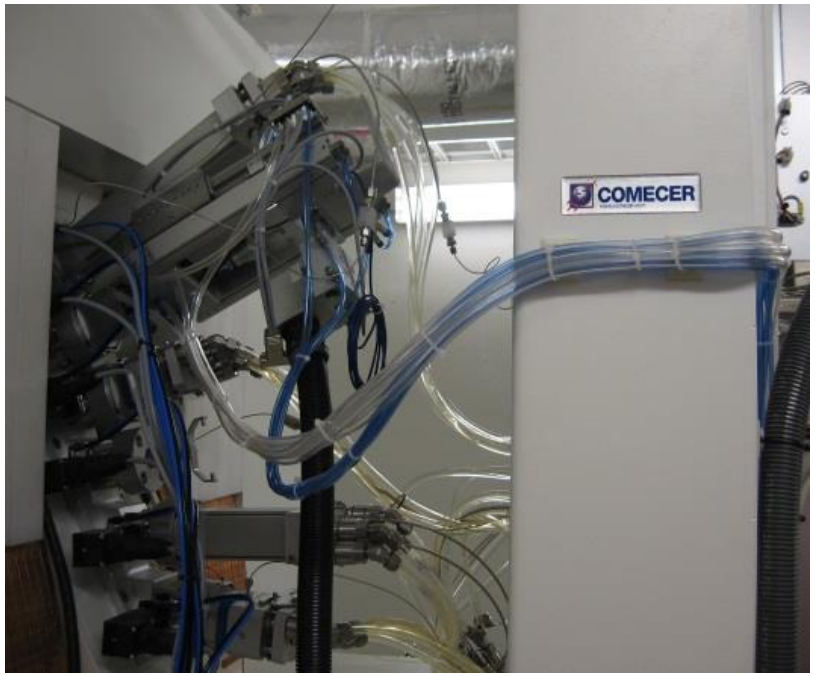




Target System - PTS



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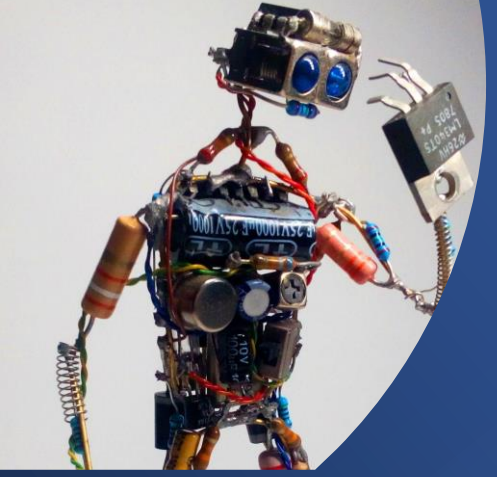
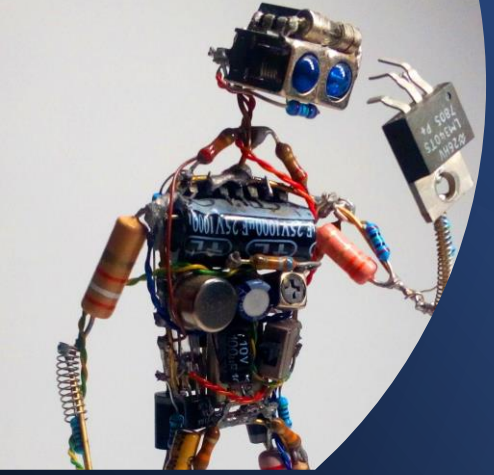
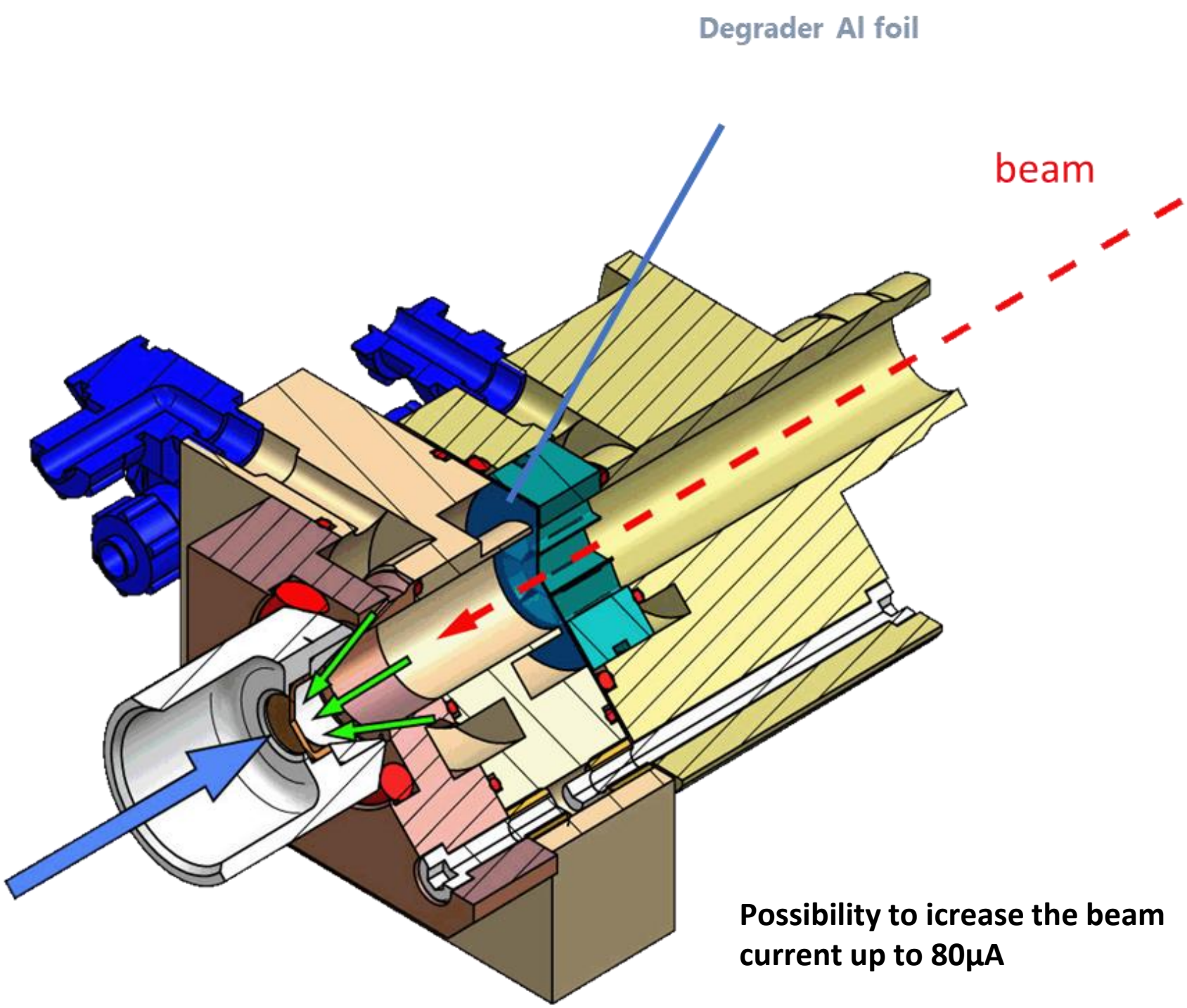


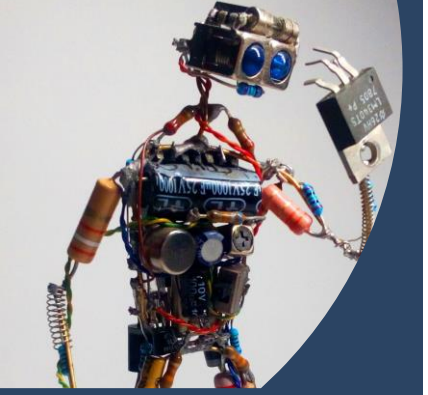
Cooling system



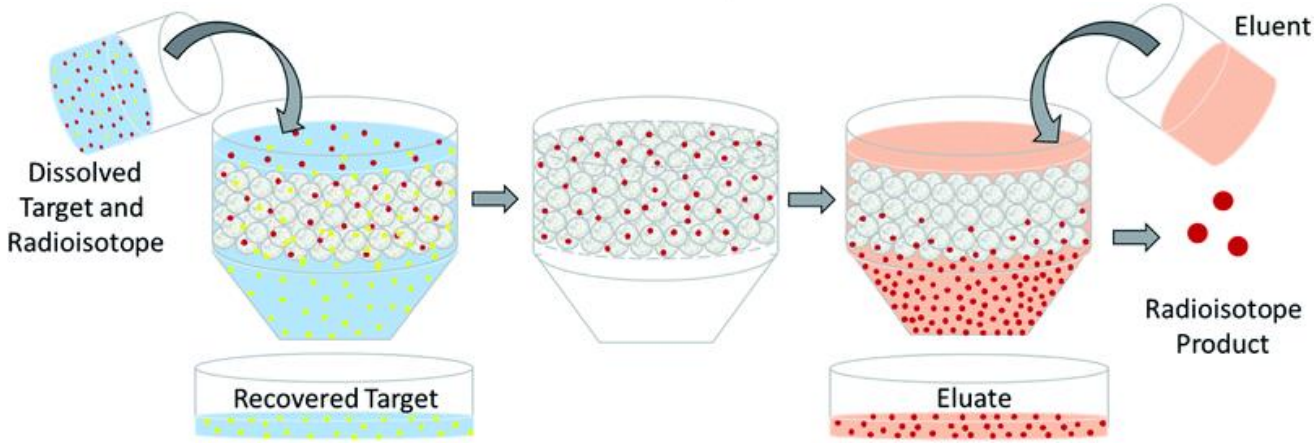
Cooling system



Possibility to icrease the beam current up to 80µA

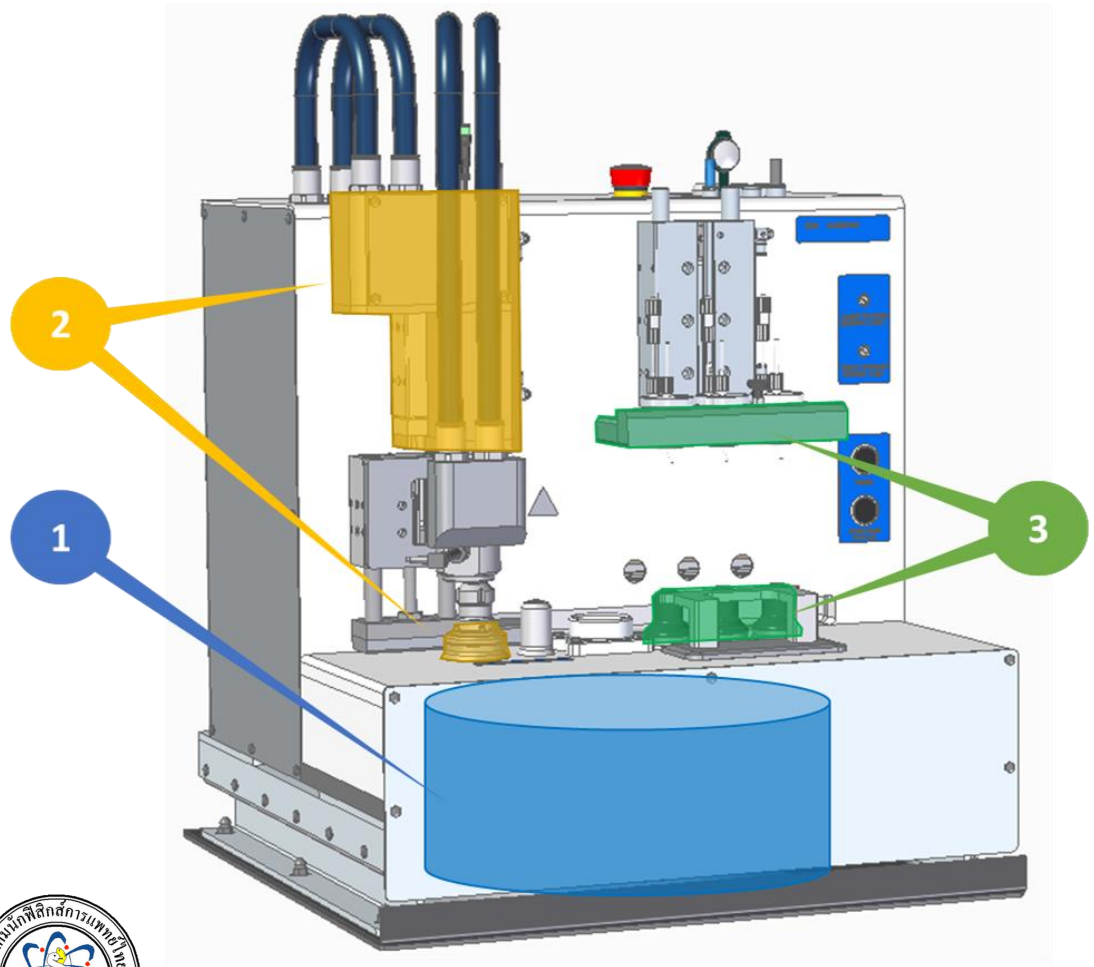


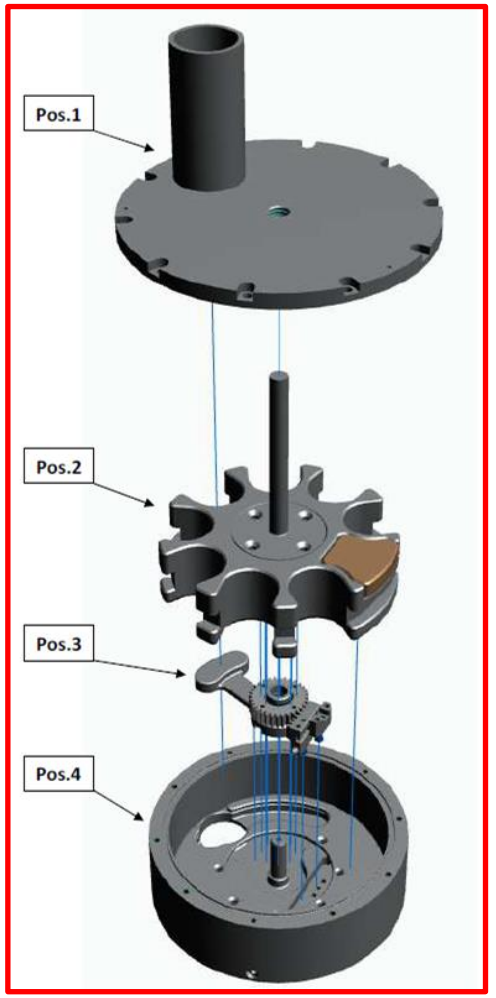
MODULES: TADEO-PRF & EDS



George, K J H et al. “Expanding the PET radioisotope universe utilizing solid targets on small medical cyclotrons.” *RSC advances* vol. 11,49 31098-31123. 21 Sep. 2021, doi:10.1039/d1ra04480j

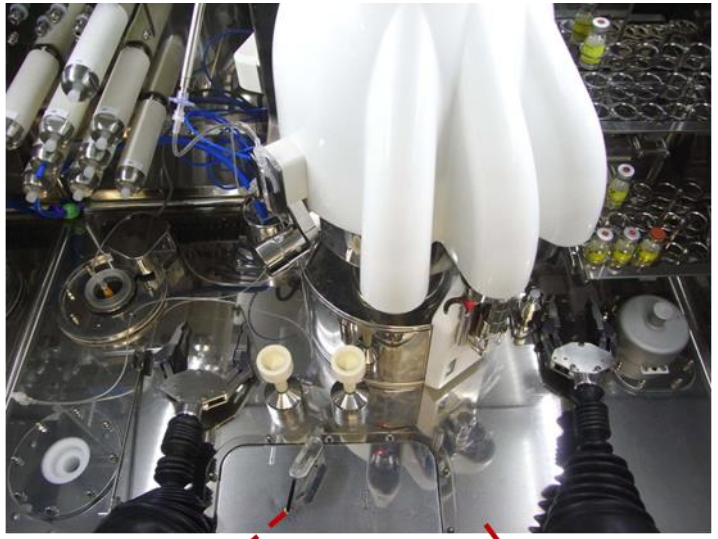
Alceo 4.0

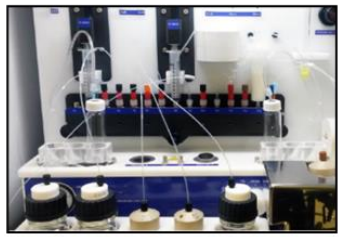


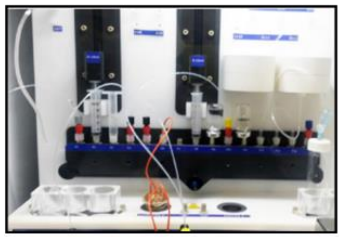


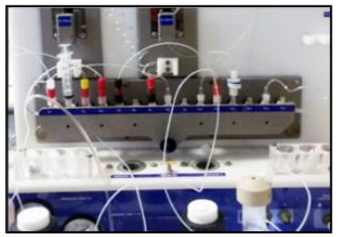
1. **INTEGRATED ROTATING STORAGE FOR THE SHUTTLES**
2. **SCREW\UNSCREW HEAD FOR THE NEW SHUTTLE**
3. **7 DISSOLUTION STATIONS**

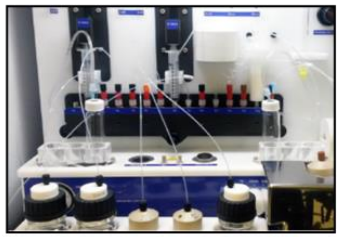
TADDEO-PRF



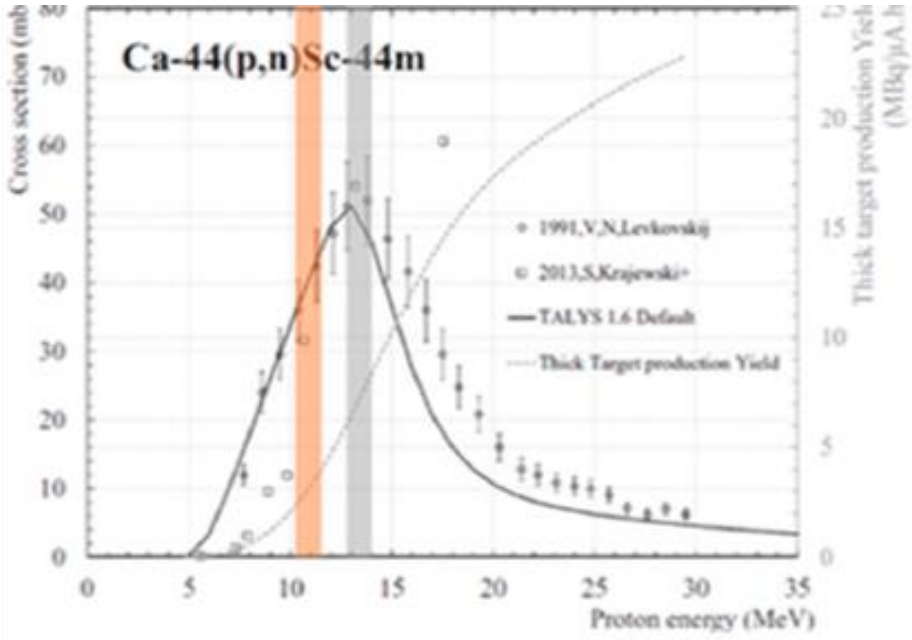

64Cu/61Cu Production kit


45Ti/89Zr Production kit

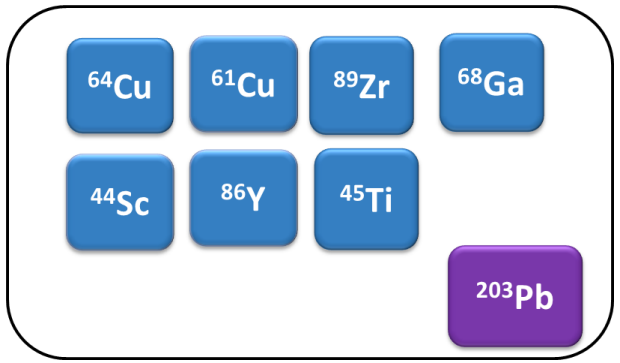

68Ga Production kit


44Sc/86Y Production kit

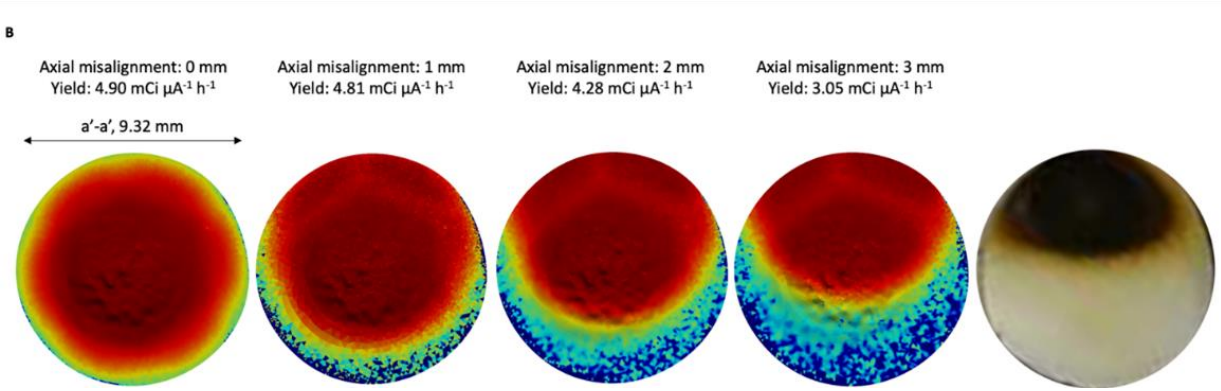
SHUTTLE



- **UNIVERSAL SHUTTLE FOR ELECTROPLATING, POWDER CHEMISTRY OR COMMERCIAL FOIL!**
- **INTEGRATED DEGRADER FOIL**
- **LARGER PLATING**



Electroplating



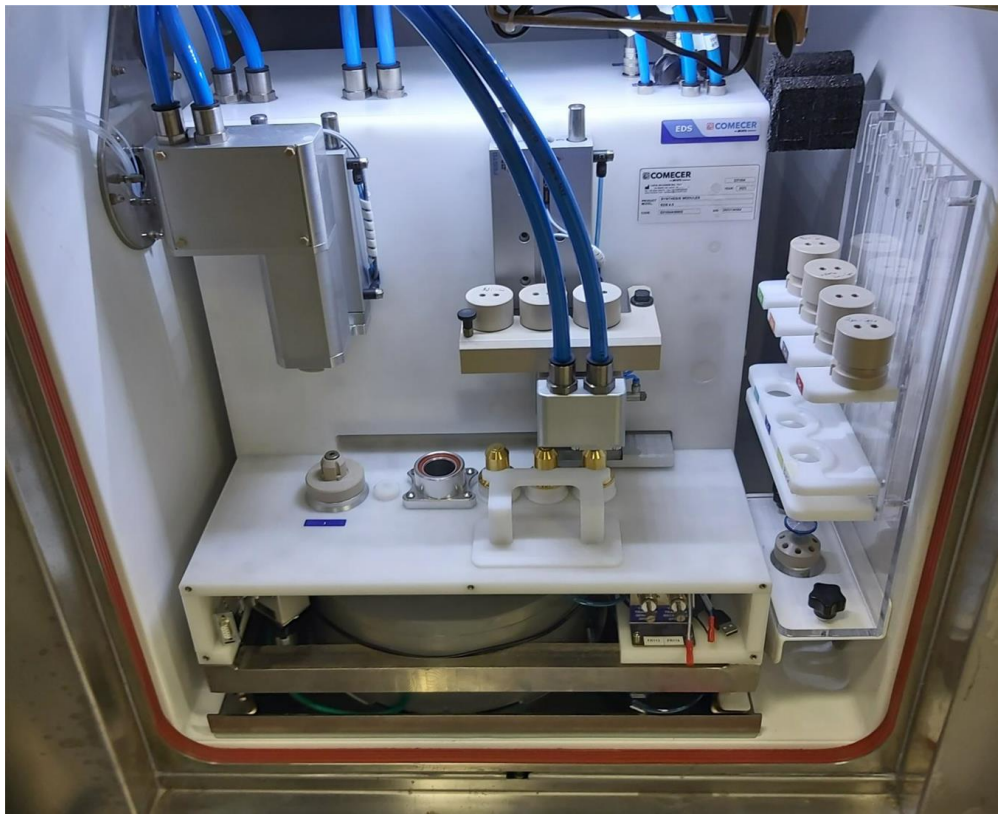
Isolan L, Malinconico M, Tieu W, et al. A digital twin for ^{64}Cu production with cyclotron and solid target system. *Sci Rep*. 2022;12(1):19379. Published 2022 Nov 12. doi:10.1038/s41598-022-23048-5

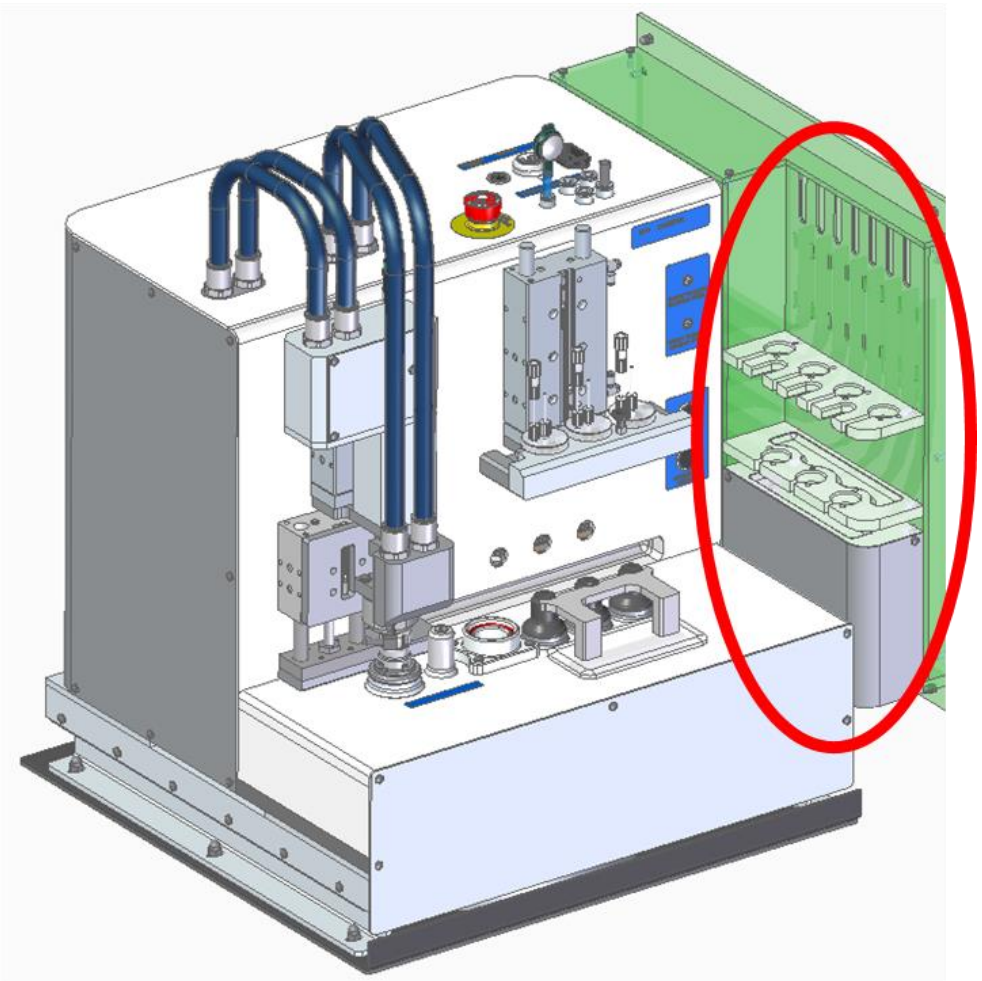
7 DISSOLUTION STATIONS

^{64}Cu ^{61}Cu ^{89}Zr ^{68}Ga

^{44}Sc ^{86}Y ^{45}Ti

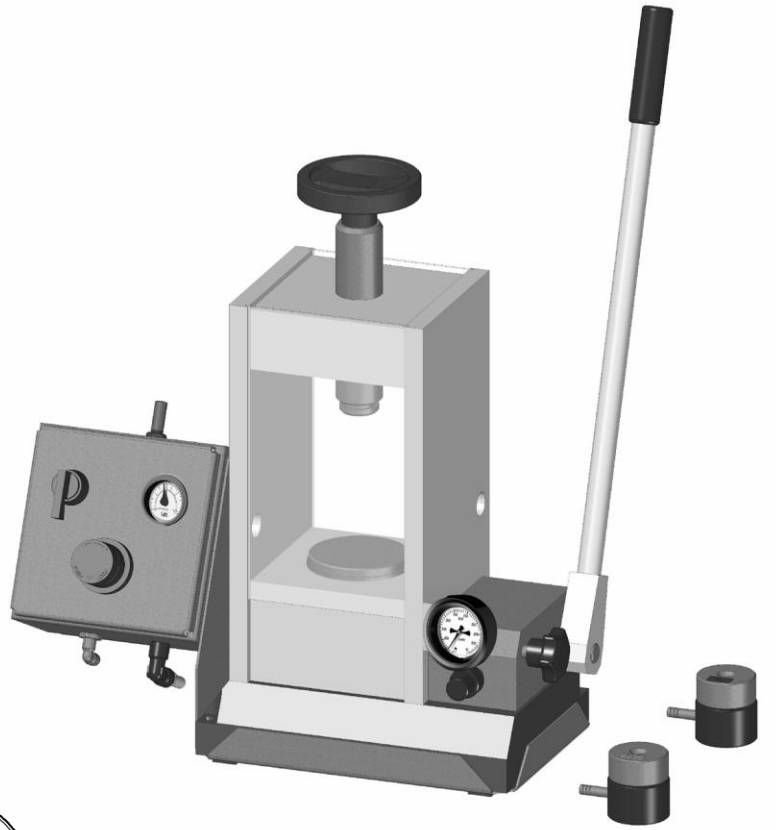
^{203}Pb





How to prepare the target(s)…

Powder compressing station

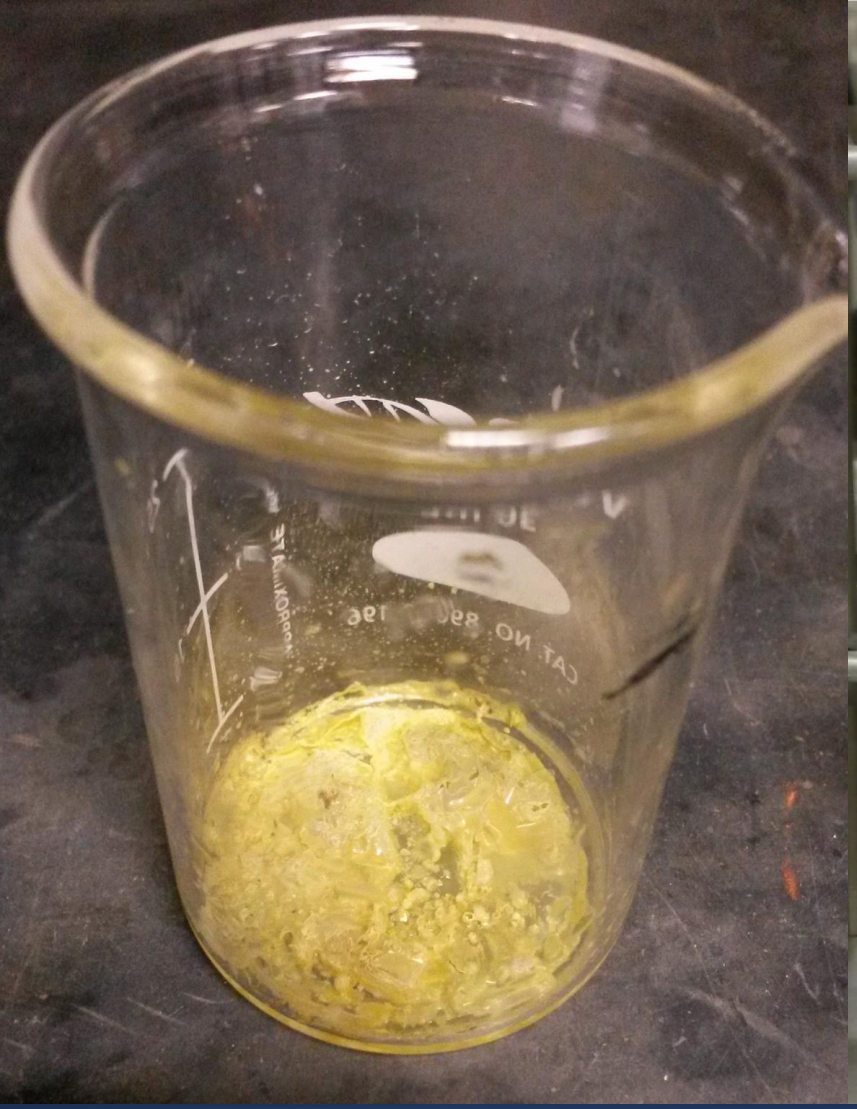


^{44}Sc ^{86}Y

^{203}Pb

External plating module

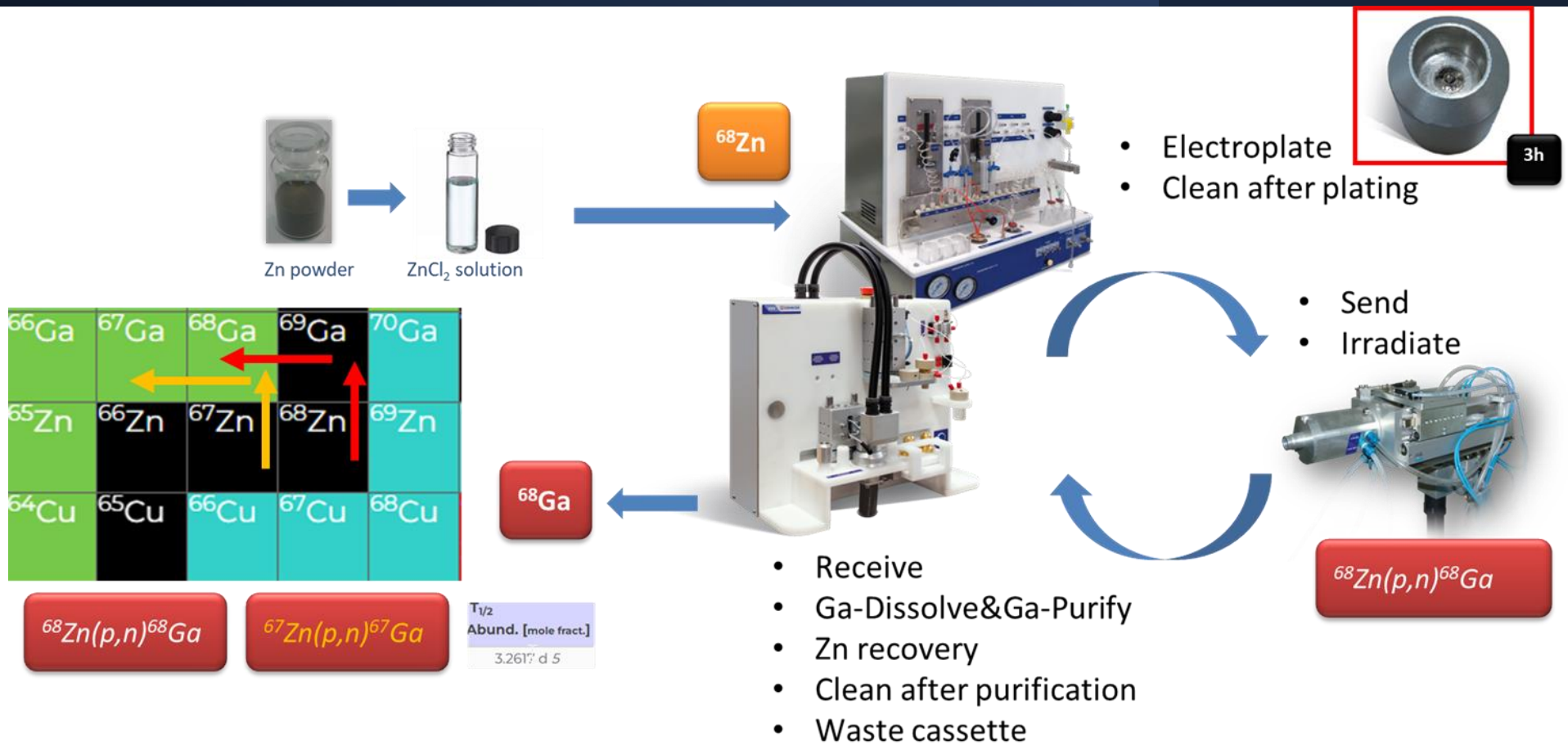
^{64}Cu ^{61}Cu ^{68}Ga



Possibility to recover the enriched material!

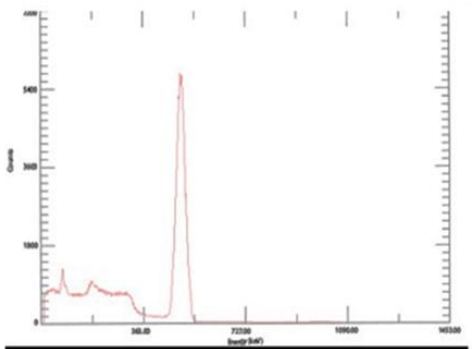
Product Video

^{68}Ga Production

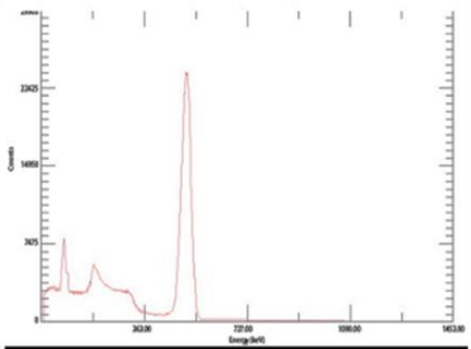


- 5mL Gallium Chloride in HCl 1M
- Expectd saturation yield 45mCi/uA (max current 35uA)

Performances



Gamma analysis of Ga-68 eluted from generator



Gamma analysis of Ga-68 produced by Comecer ALCEO

GALLIUM (68Ga) CHLORIDE SOLUTION FOR RADIOLABELLING

Gamma analysis comparison ALCEO-GENERATOR production

European Pharmacopoeia

- Half life: 62-74min

Batch No. Ga test 100 uL

	Time (hh:mm:ss)	Activity (MBq)	Time (min)	ln(At/A0)
Enter 1st data point→	14:16:45	23.200	0.0	0.0000
Enter 2nd data point→	14:18:45	22.700	2.0	-0.0218
Enter 3rd data point→	14:20:46	22.300	4.0	-0.0396
Enter 4th data point→	14:22:47	21.800	6.0	-0.0622
Enter 5th data point→	14:24:47	21.400	8.0	-0.0808

Regression Analysis:

Slope	-0.01010
R-squared	0.99882

Results:

Theoretical Half life	67.629 min
BP Specification	62-74 min
Calculated Half life	68.64 min
Difference	1.5 %

Test	Result	
Radionuclidic purity	% ^{67}Ga at EOP = 0,019%	
pH	<2	
Fe (ppb)	Prod1: 332	Prod2: 1350
Zn (ppb)	Prod1: 371	Prod2: 5130

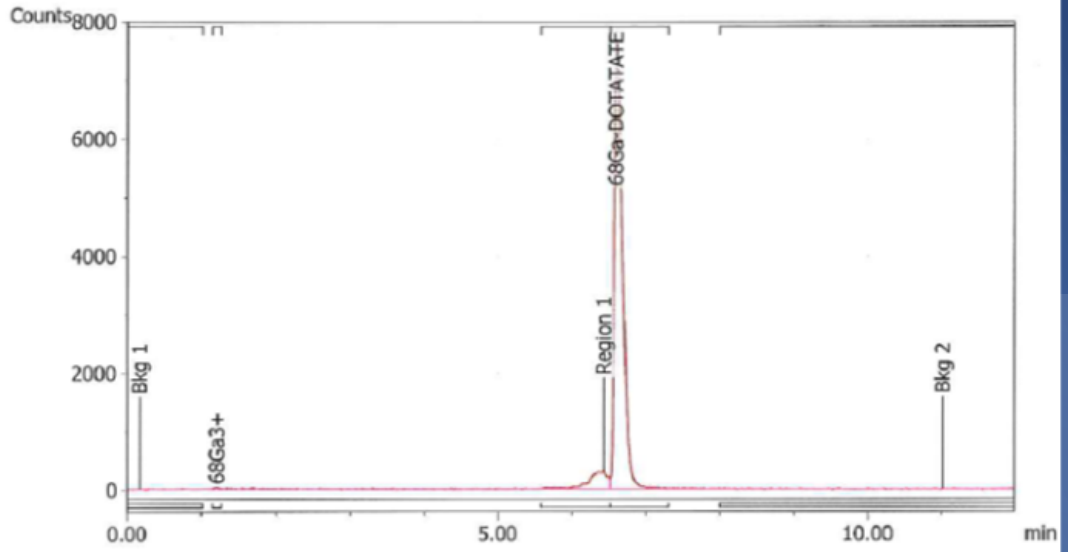
GALLIUM (68Ga) CHLORIDE SOLUTION FOR RADIOLABELLING

European Pharmacopoeia

Gallium-68: min 99.9 %of the total radioactivity

- pH = max 2.
- Iron = maximum 10µg/GBq.
- Zinc = maximum 10µg/GBq.

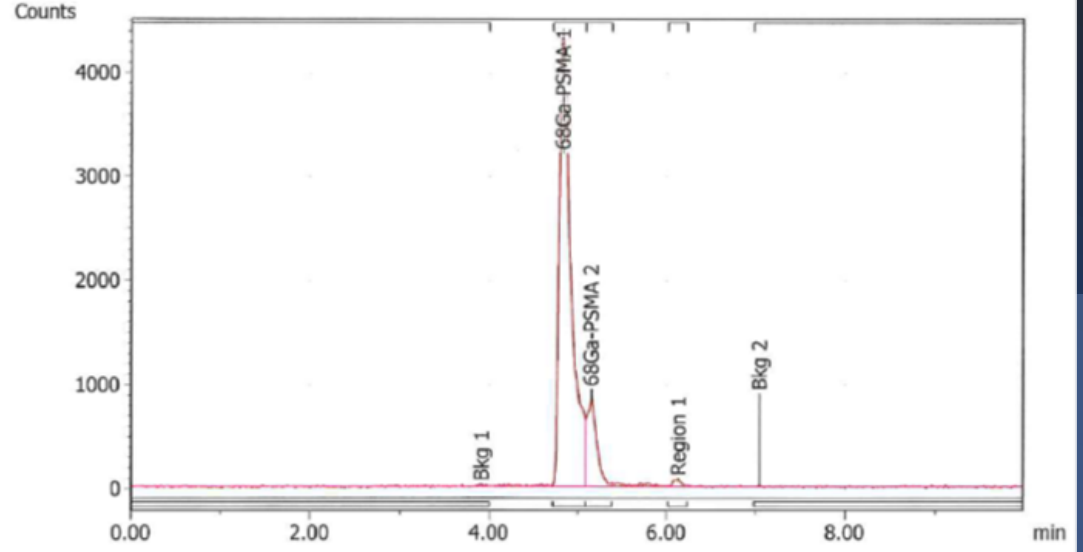
Radiodetector (FlowRAM) Results:
Chromatogram: ^{68}Ga



Region Table:

Name	Start (min)	End (min)	Retention (min)	Area (Counts)	%ROI (%)	Signal to Noise Ratio
Bkg 1	0.00	1.02	0.17			
68Ga3+	1.15	1.27	1.22	162	0.25	2.47
Region 1	5.58	6.52	6.43	5572	8.49	25.61
68Ga-DOTATATE	6.52	7.30	6.60	59861	91.26	713.57
Bkg 2	8.00	11.98	11.02			
3 Peaks				65595	100.00	

Radiodetector (FlowRAM) Results:
Chromatogram: ^{68}Ga



Region Table:

Name	Start (min)	End (min)	Retention (min)	Area (Counts)	%ROI (%)	Signal to Noise Ratio
Bkg 1	0.00	4.00	3.92			
68Ga-PSMA 1	4.72	5.08	4.83	40095	84.40	304.52
68Ga-PSMA 2	5.08	5.38	5.15	6929	14.58	56.97
Region 1	6.02	6.23	6.13	483	1.02	4.76
Bkg 2	6.98	9.98	7.05			
3 Peaks				47507	100.00	

	SYNTHESIS			HPLC	
Products	EOS activity (MBq)	Synthesis yield	Decay corrected yield	Radiochemical purity	Free $^{68}Ga^{3+}$
DOTATATE	888	76,0%	88,6%	91,3%	0,25%
PSMA	570	79,2%	89,6%	99,0%	Not detected

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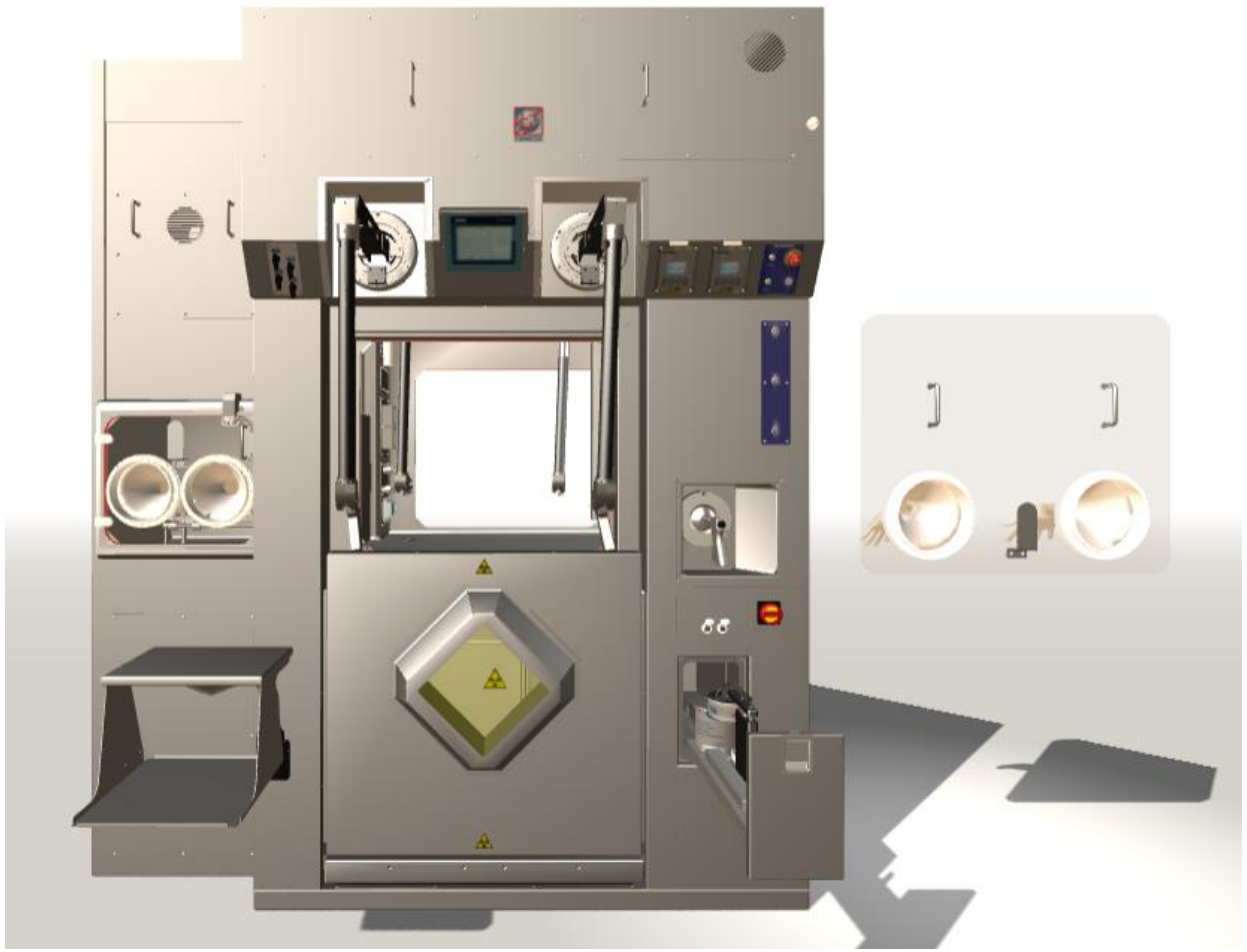
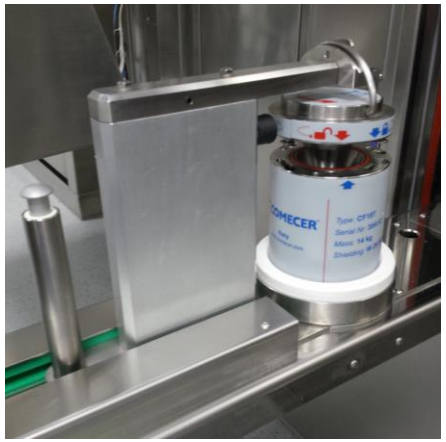
SAHMRI
South Australian Health & Medical Research Institute

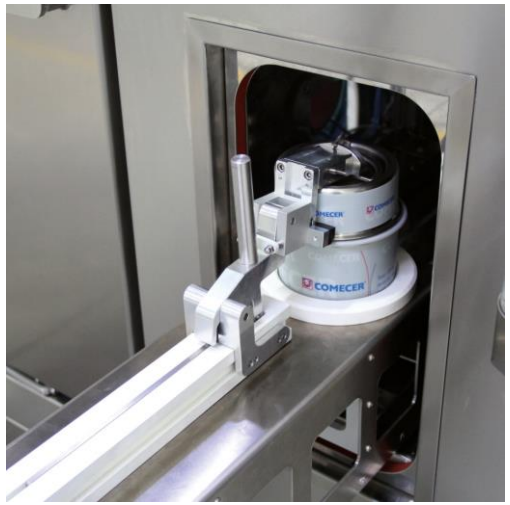
RADIOLABELING - MIP HOT CELL

RADIOLABELING - MIP HOT CELL

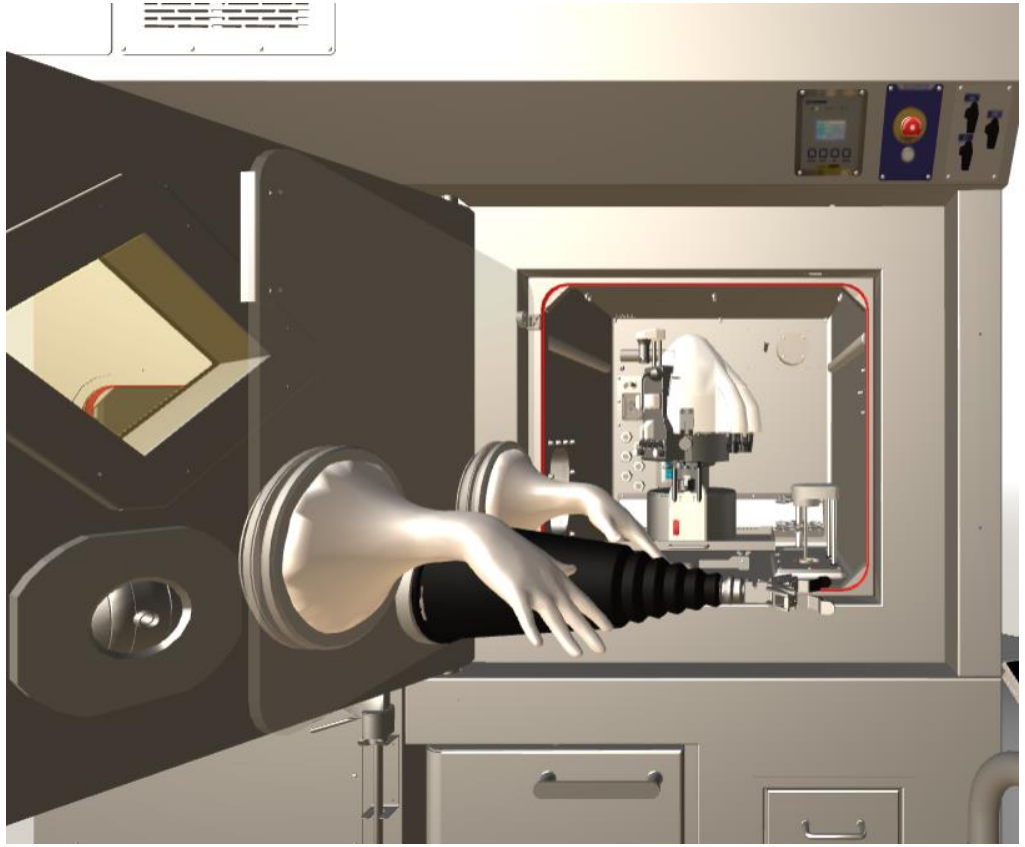




DISPENSING HOT CELL - PHAEDRA



DISPENSING HOT CELL - PHAEDRA



Radiopharmaceutical injection

Why an automatic radiopharmaceutical injector?

Significant staff exposure is generally expected during PET-and PET/CT applications. Whole-body doses as well as extremity doses are usually higher per procedure compared with SPECT applications. Dispensing individual patient doses and manual injection involves high extremity doses even when heavy weighted syringe shields are used. In some cases the external radiation causes an exposure to the fingertips of more than 500 mSv y^{-1}, which is the yearly limit. Whole-body doses per procedure are relatively lower compared with extremity doses and are generally spread over the entire procedure (Guillet, B.,

TABLE 4
Mean ± SD (n = 10) Dose Rates Measured by TLD Positioned Either on Syringe Shield Inside Injector or on External Face of Injector

TLD location	Dose rate (mSv/h)	Dose rate (mSv/h) per MBq
Syringe	58.7 ± 13	0.19 ± 0.02
Injector	0.047 ± 0.062	0.00017 ± 0.000014

REFERENCES:

Covens P, Berus D, Vanhavere F, Caveliers V. The introduction of automated dispensing and injection during PET procedures: a step in the optimisation of extremity doses and whole-body doses of nuclear medicine staff. Radiat Prot Dosimetry. 2010 Aug;140(3):250-8. doi: 10.1093/rpd/ncq110. Epub 2010 Mar 23. PMID: 20335185.

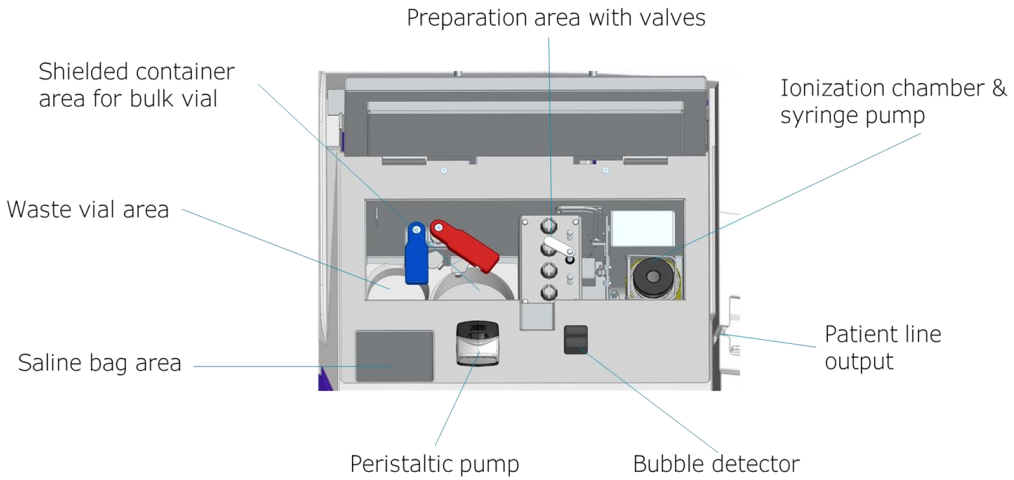
Guillet B, Quentin P, Waultier S, Bourrelly M, Pisano P, Mundler O. Technologist radiation exposure in routine clinical practice with 18F-FDG PET. J Nucl Med Technol. 2005 Sep;33(3):175-9. PMID: 16145226.

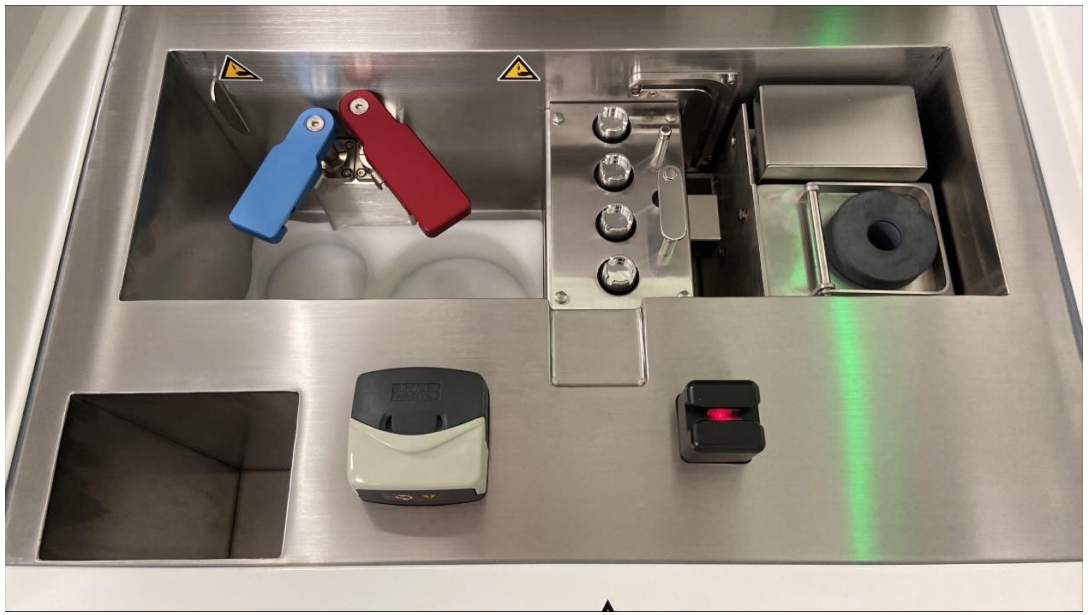
IRIS

IRIS – automatic radiopharmaceutical injector

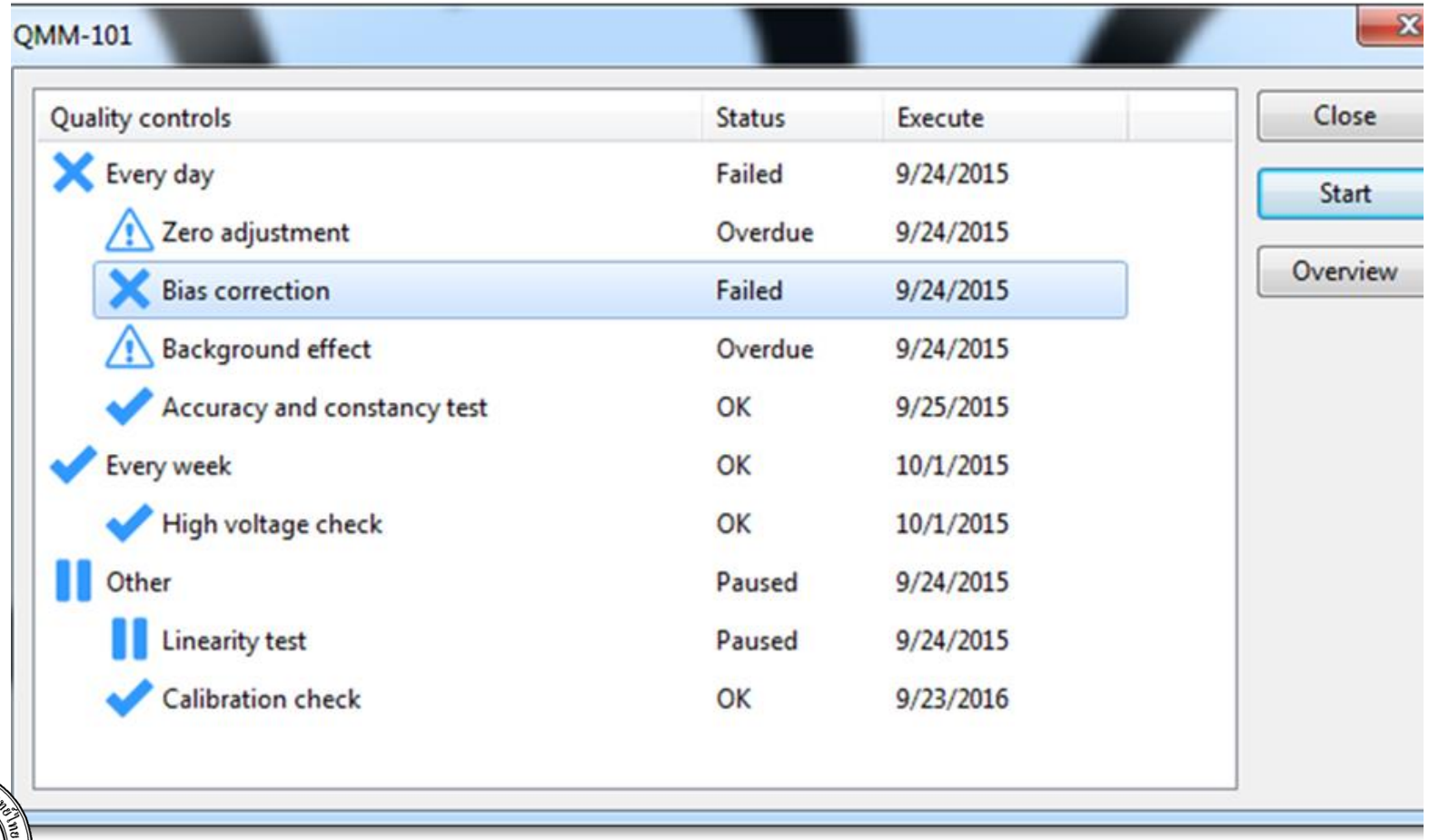
Weight	kg	330 (+/-5)
External dimensions (handle open)	cm	63,5 x 114 x 96,5 (w x d x h)
External dimensions (handle closed)	cm	63,5 x 90 x 81 (w x d x h)

Main components



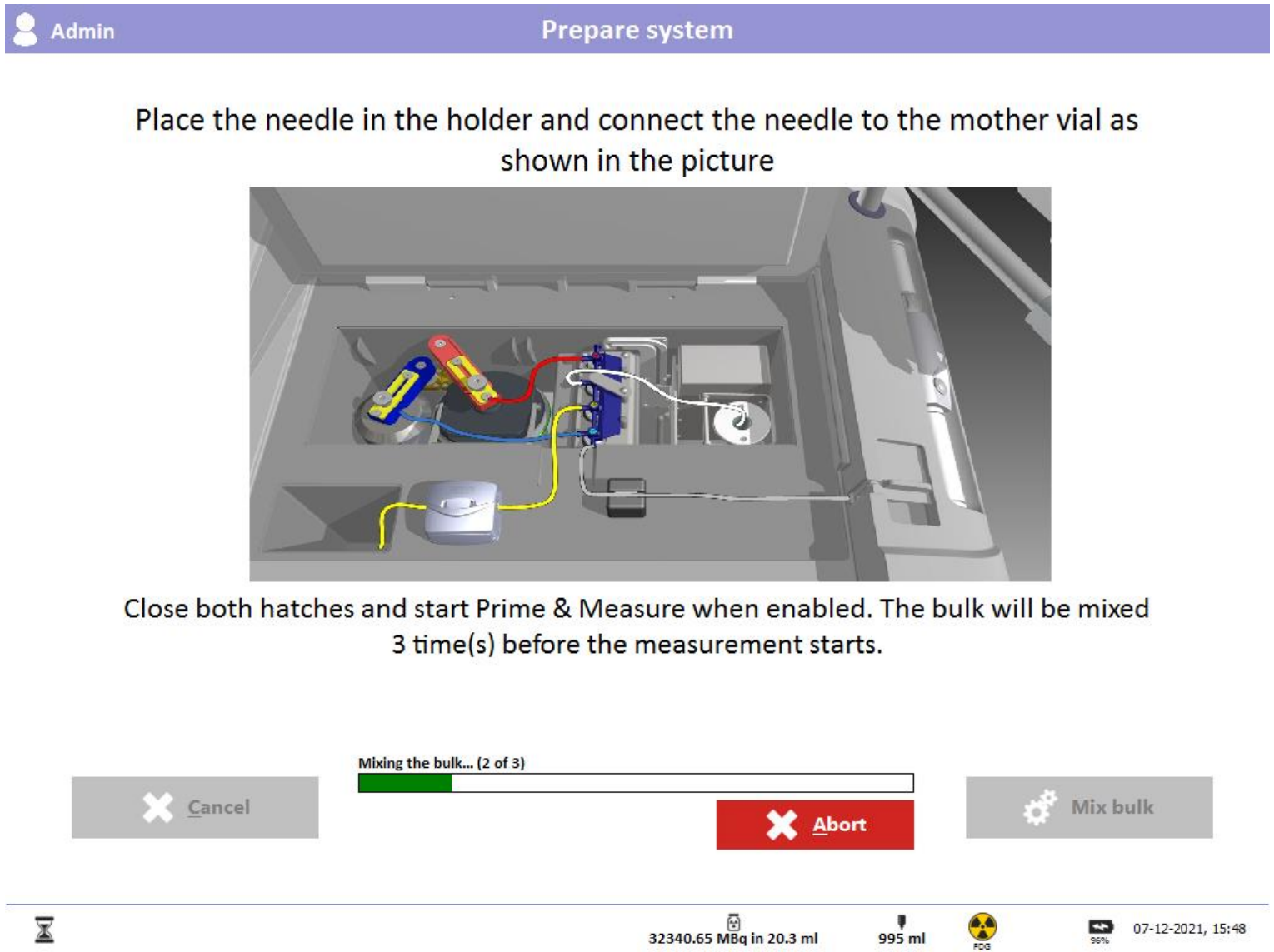


DC Quality Control



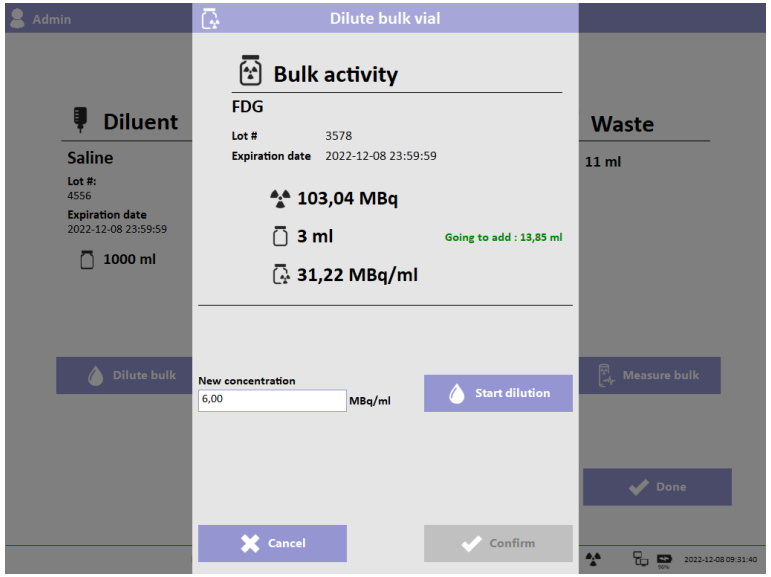
- QMM is an integrated module in the IRIS software suitable for executing and keeping quality controls updated.
- The QMM will give a pop-up on the HMI when a quality check is required

System preparation

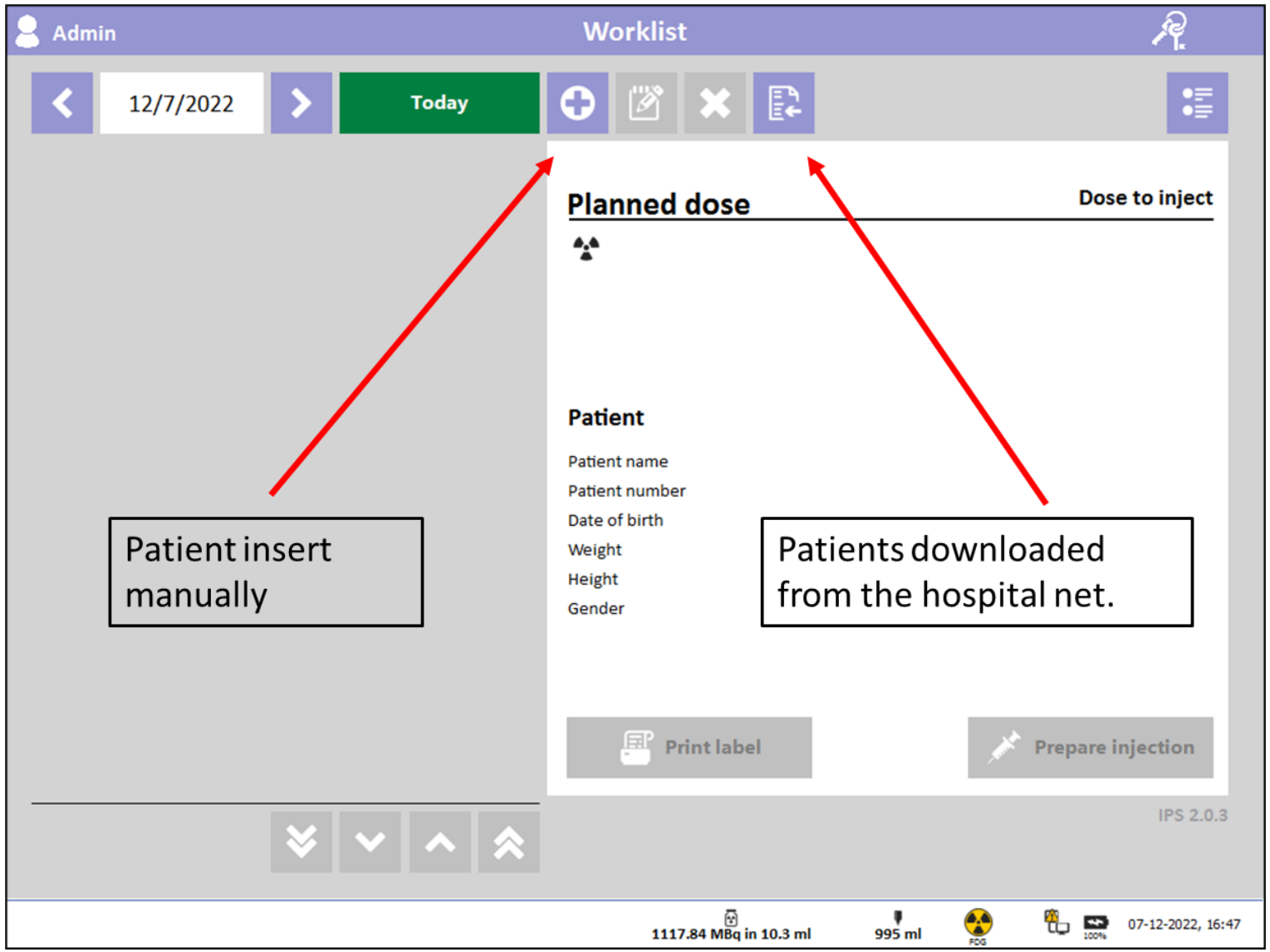


Multi-dose vial management

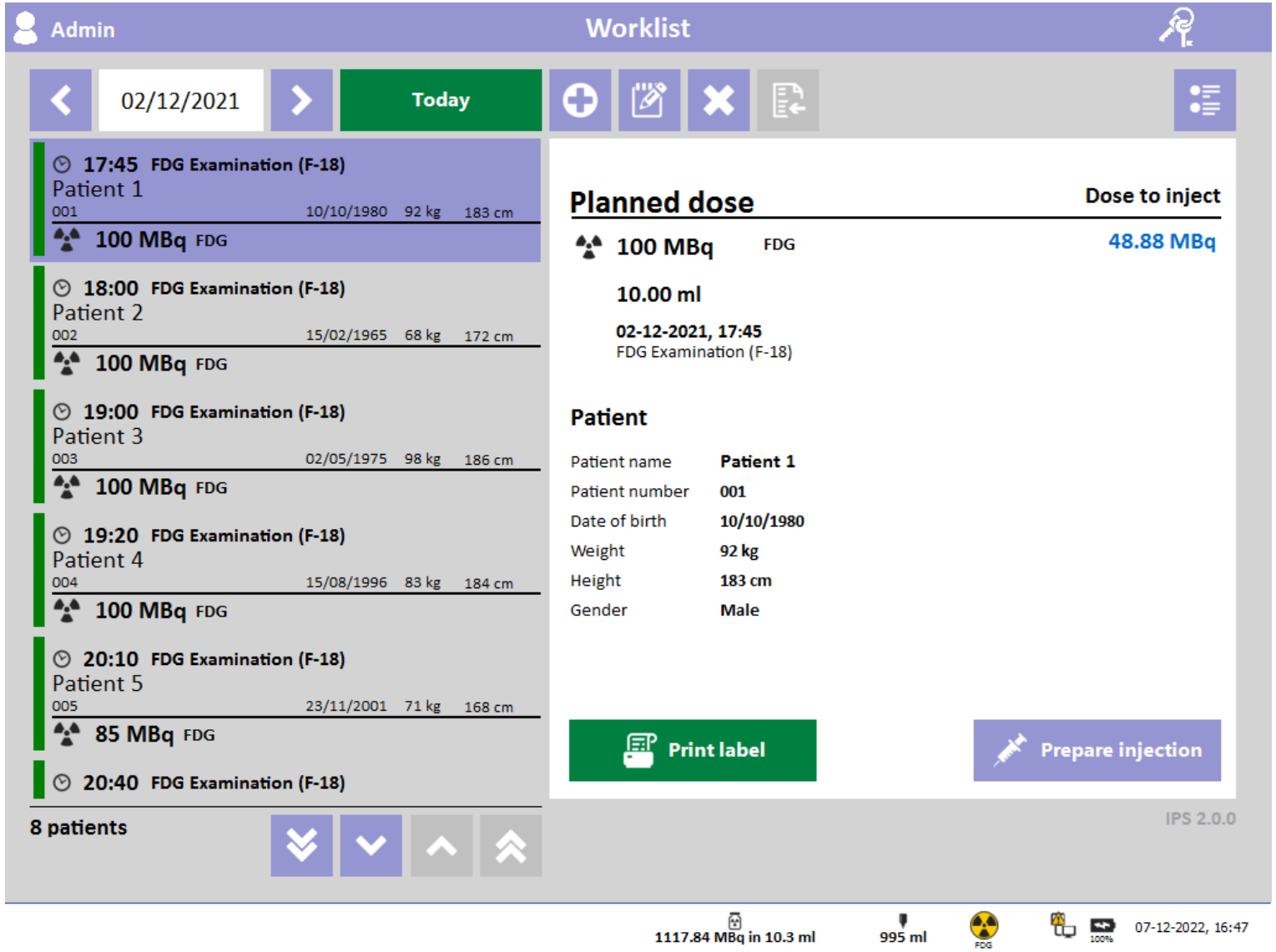
- Measurement of multi-dose vial activity/concentration
- Dilution of multi-dose vial in bulk vial



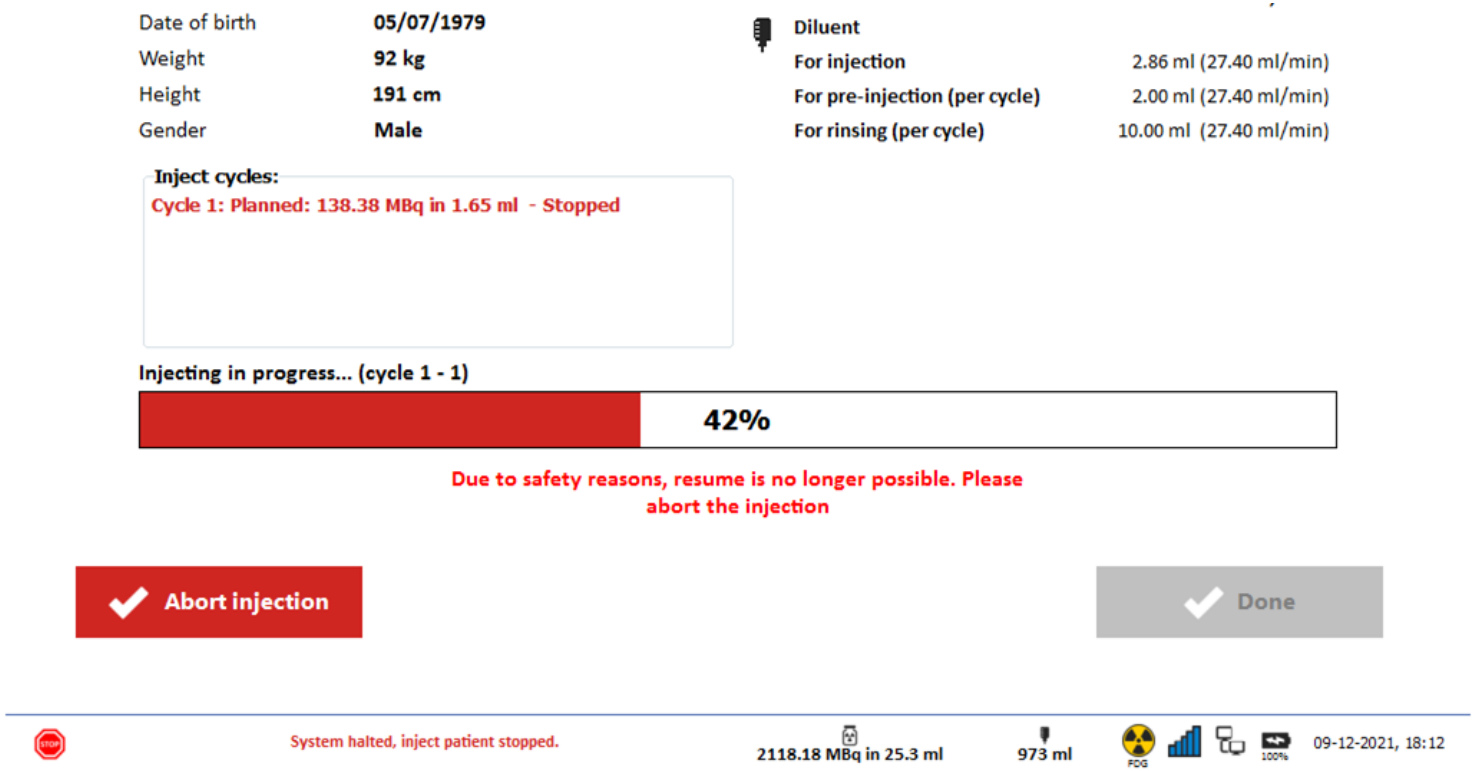
Patient selection



Patient selection

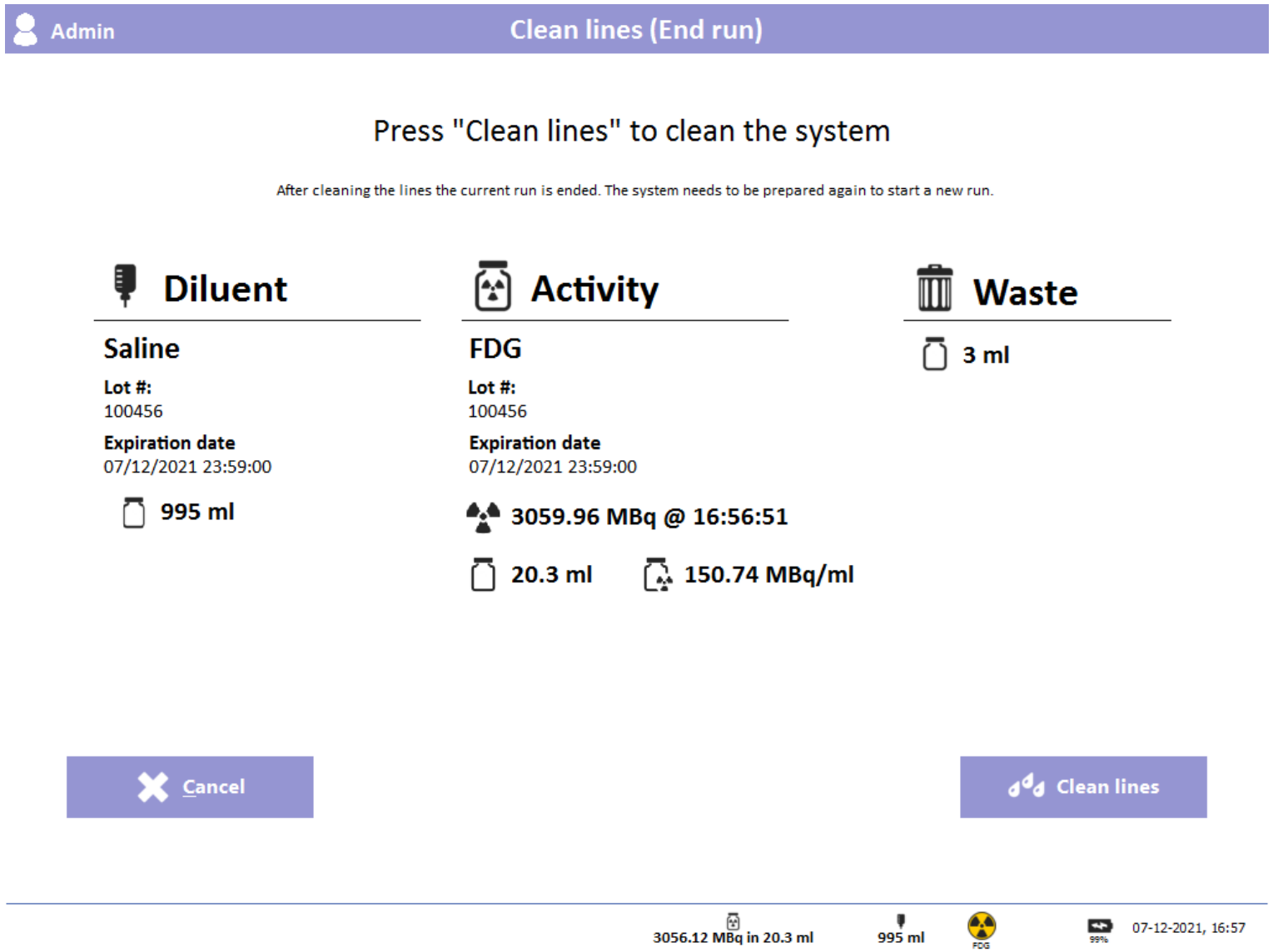


Safety system

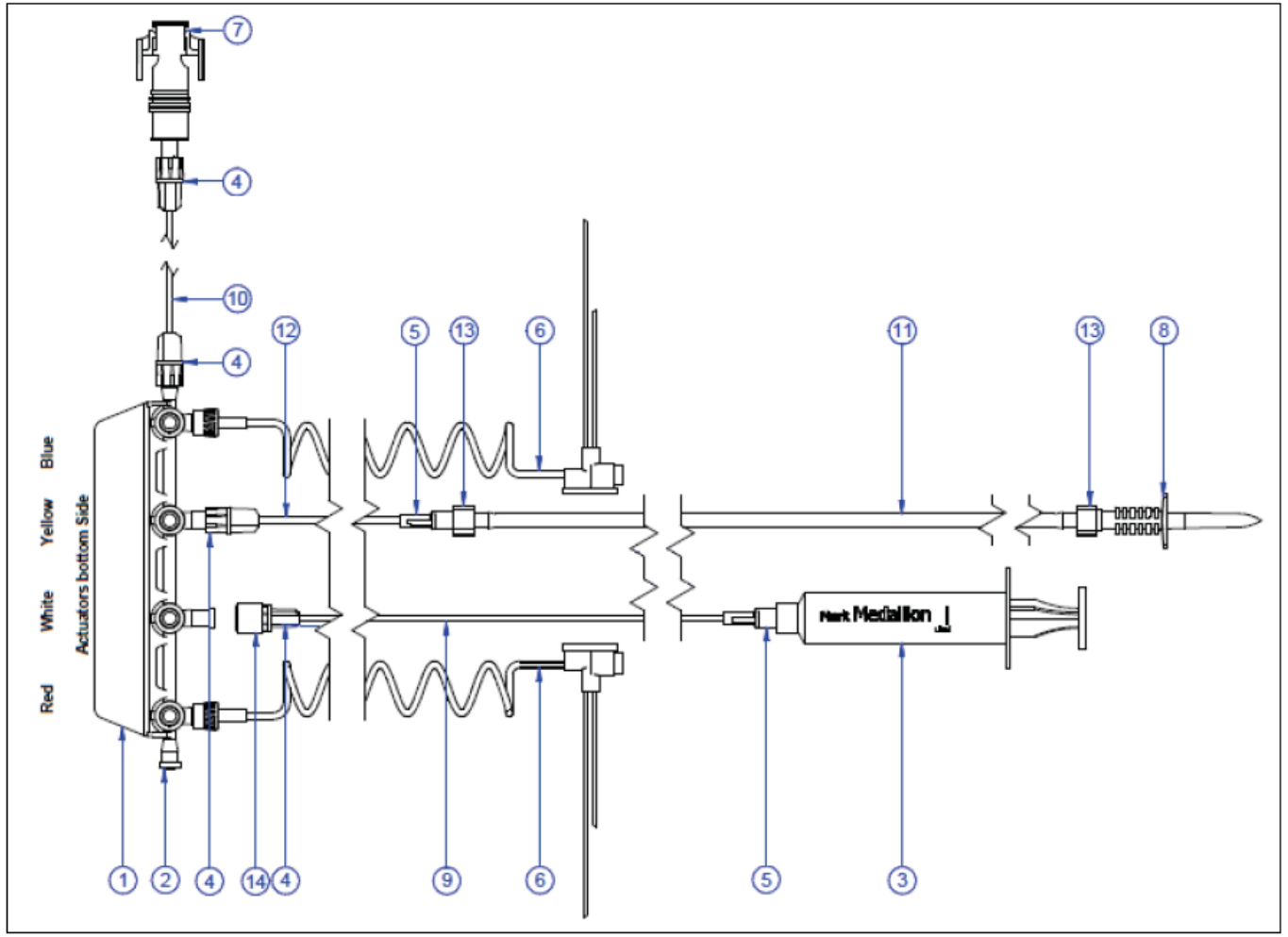


- Increase in pressure detection
- During test injection
- During radiopharmaceutical injection

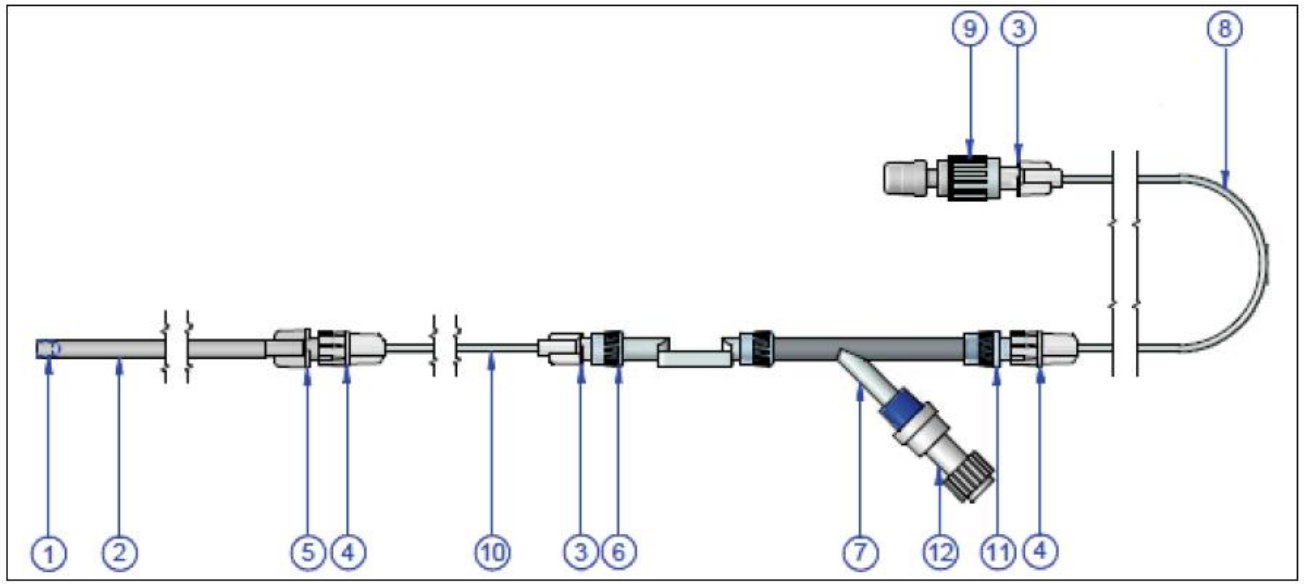
Clean line procedure



Disposable main kit



Batch kit



Patient set

Disposable patient kit

Label management

- The system is equipped with a label printer, connected to the operator panel, which prints self-adhesive labels of various lengths according to the layout and information required. The layout is adjustable.

Radio Pharmaceutical name

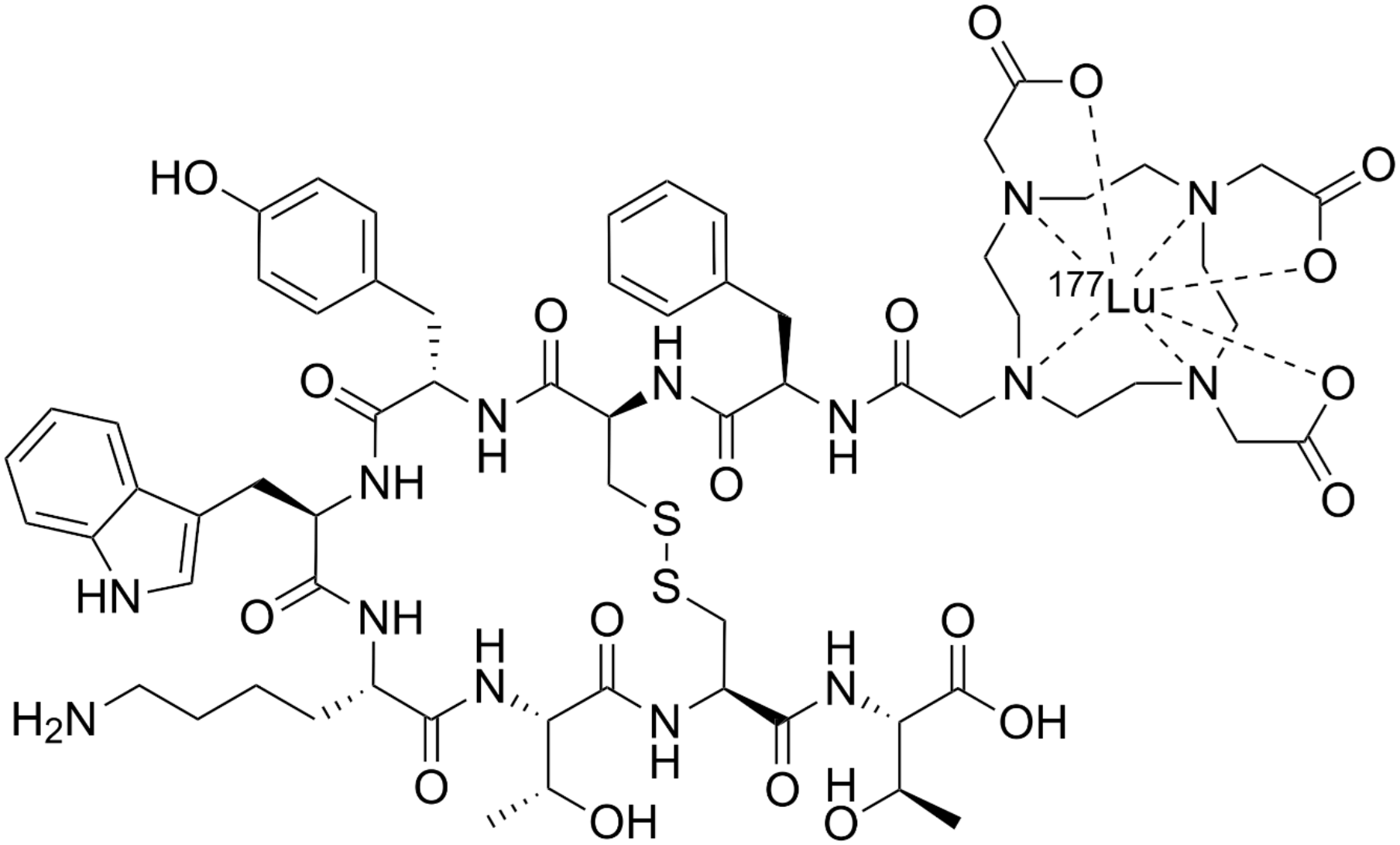
Patient: Patient name

Patient number 01-10-1974 112,5 kg 195 cm

Exam: Examination name

07-10-2015 10000 MBq @ 11:39 20 ml

IRIS Injector www.comecer.com



LUTATHERA® injection experience

National Cancer Institute Pascale Foundation

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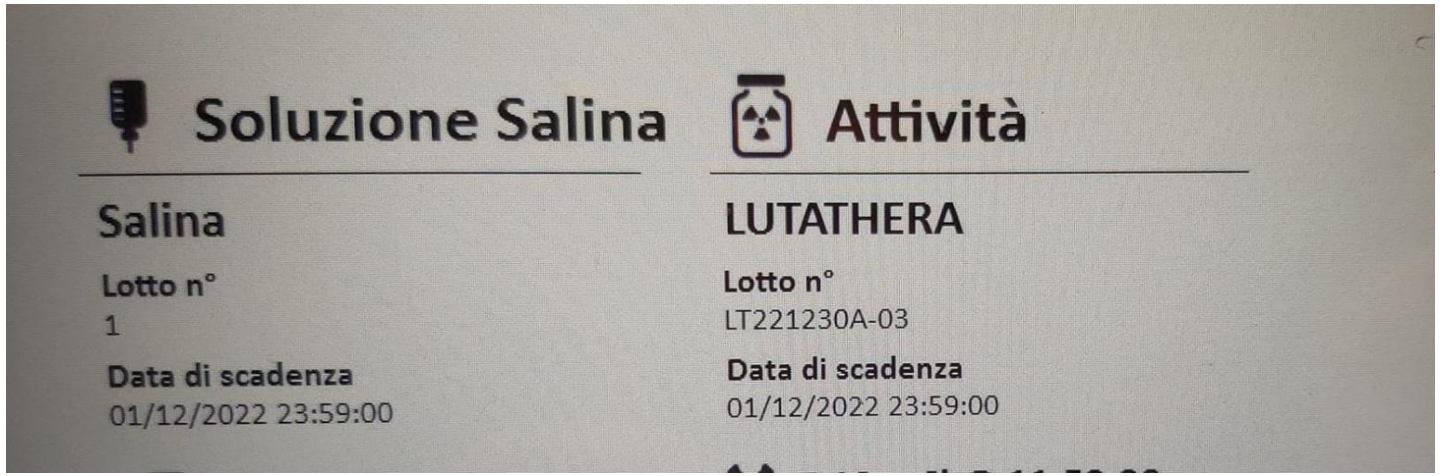

Radioactivity injection flow: 15mL\min
Saline injection flow: 10mL\min

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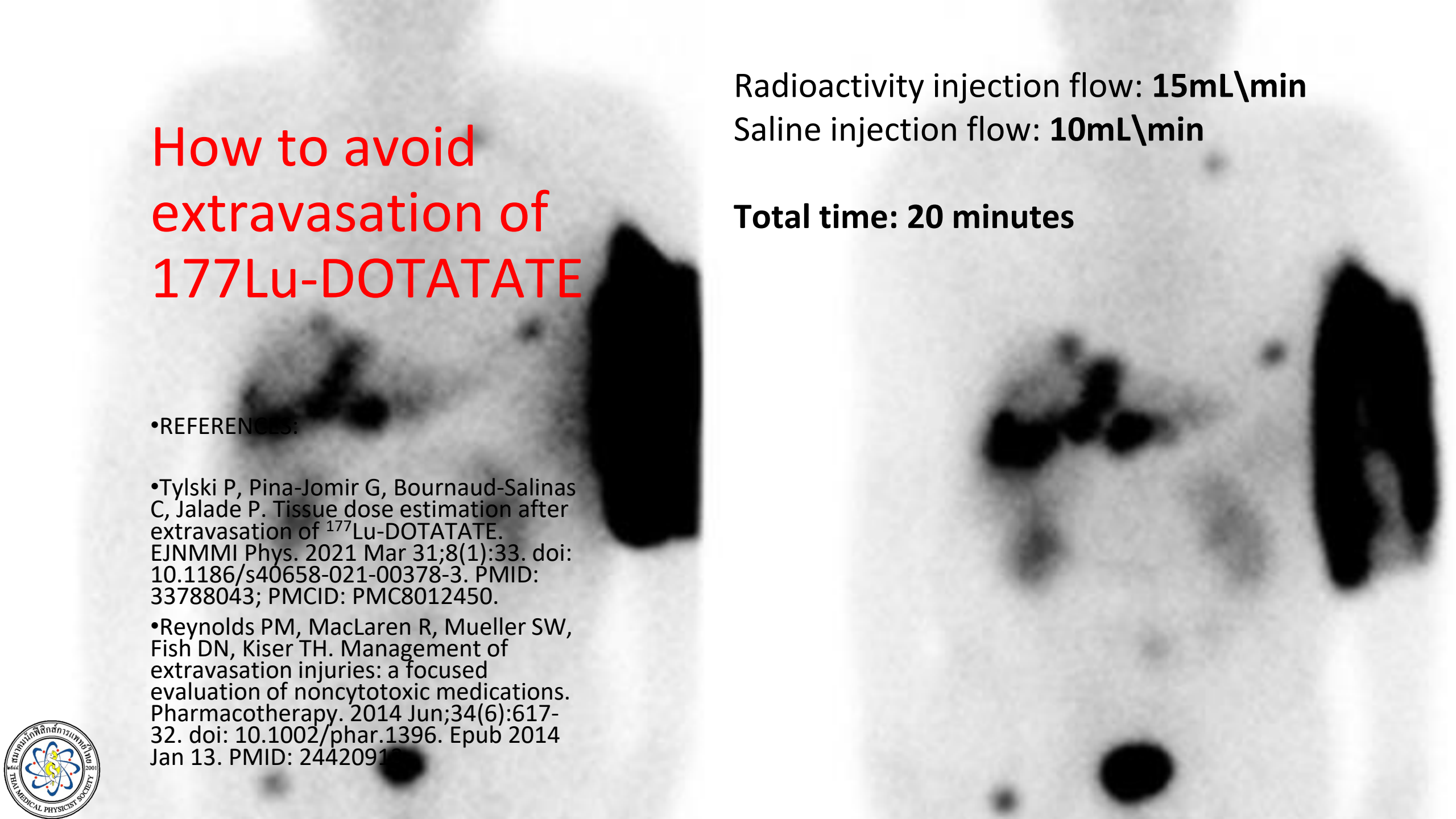
How to avoid extravasation of 177Lu-DOTATATE

Radioactivity injection flow: **15mL\min**
Saline injection flow: **10mL\min**

Total time: 20 minutes



•REFERENCES:

•Tylski P, Pina-Jomir G, Bournaud-Salinas C, Jalade P. Tissue dose estimation after extravasation of ^{177}Lu-DOTATATE. EJNMMI Phys. 2021 Mar 31;8(1):33. doi: 10.1186/s40658-021-00378-3. PMID: 33788043; PMCID: PMC8012450.

•Reynolds PM, MacLaren R, Mueller SW, Fish DN, Kiser TH. Management of extravasation injuries: a focused evaluation of noncytotoxic medications. Pharmacotherapy. 2014 Jun;34(6):617-32. doi: 10.1002/phar.1396. Epub 2014 Jan 13. PMID: 2442091

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www.comecer.com

marketing@comecer.com

mmalinconico@comecer.com

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